THE FOETAL CIRCULATION

THE FOETAL CIRCULATION

AND CARDIOVASCULAR SYSTEM, AND THE CHANGES THAT THEY UNDERGO AT BIRTH

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TO

SIR JOSEPH BARCROFT

AND

DR DONALD H BARRON



THIS BOOK IS PRODUCED
IN COMPLETE CONFORMITY WITH THE
AUTHORIZED ECONOMY STANDARDS

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PREFACE

THIS book contains an account of our own foetal studies, together with a summary of the related findings of other workers Before going on to discuss it in detail, we wish to make three major acknowledgements to Lord Nuffield, to Dr E C Amoroso, and to our Publishers respectively

Lord Nuffield presented to Oxford University, for the use of its Medical School the beautiful late 18th century building in which we are privileged to work he also provided most of our apparatus, and he has shown a personal interest in our results We are glad to have this opportunity of expressing our very considerable indebtedness to him

Dr Amoroso of the Royal Veterinary College, has provided or collected, from 1940 onwards, most of the comparative anatomical specimens which we have dissected, and he has himself dissected many others (e g , those depicted in figs 48 121 *b* to *f* 122, and 128) In addition, he has been responsible for almost all the histological work and has supervised the production of the photographs and drawings reproduced as figs 39, 40 48, 99–100 102–106, 121 *b* to *f* 122 and 147 We wish to acknowledge here not only the very great assistance he has so freely given us in the preparation of material for this book, but also the very happy collaboration which we have enjoyed with him during the last four years We should also like to pay a tribute to his artistry in macro and micro dissection It was, earlier, our hope that his name would appear with ours on the title page of this book but a succession of untoward events made this impossible so we must demonstrate, in this alternative way, our appreciation of his efforts

Of our Publishers wholehearted co operation with us we cannot speak too highly To Mr Basil Blackwell and Mr Henry Schollick in particular we are most grateful, and we realize how fortunate are the authors whose works they undertake to produce

The foetal studies at the Nuffield Institute were initiated in 1937, when Sir Joseph Barcroft and Dr D H Barron asked if we would co operate, with our cineradiographic techniques, in the solution of their problem namely, the determination of the time of functional closure of the ductus arteriosus [1] We agreed very readily, and two seasons of collaboration gave our combined teams not only the answer to the immediate question but also the first direct records of the circulation in the intact foetus, delivered by Caesarean section [2] Thereafter the outbreak of war ended the pleasant partnership that we had enjoyed

[1] At the meeting of the Physiological Society on 13 March 1937 a film made by Barcroft and Barron (Experimental chronic lesions in the central nervous system of the sheep s foetus) was projected immediately before one made by Janker and Franklin (X ray cinematographic film of a dog s heart) This accidental juxtaposition of the two films suggested to Barron the new line of attack.

Priority in the idea of a radiographic recording of the foetal circulation belongs apparently to Gargiulo M (1936) Unfortunately his paper in *Riv di Chir Como* 2 has not been accessible to us but there is a brief note in *Riforma med* 1936 52 971 which reads as follows GARGIULO M *Tentativi di studio della circolazione fetale mediante impiego di raggi Rontgen* L O si propone

with our colleagues from Cambridge, and at the same time reduced our own opportunities for research In the intervals of other work, however, we have from time to time added to our experimental findings, and we have also made fairly extensive comparative anatomical studies

In as much as it was the physiological findings which led us on to re-investigate the anatomy, we have given the foetal circulation, rather than the foetal cardiovascular system, pride of place in the title of our book As our main object, in an Institute for Medical Research, is to discover more about the *human* subject, we should have liked to reproduce as a frontispiece a diagram of the *human* foetal circulation and of its changes at birth But accurate knowledge of this, based upon radiographic records, is not at present available, so we have preferred to omit a frontispiece altogether when we cannot have the one of our choice In view of the way in which our foetal researches began, the dedication of the book to Sir Joseph Barcroft and to Dr D H Barron needs no further explanation We should, however, state that the opinions and interpretations to be found in the text are, unless otherwise indicated or apparent, our own [1] In other words, if criticism can justly be levelled against anything which we have written, our erstwhile colleagues should not be held jointly responsible, for they have not seen the book during its production

In general, in the text, we have adhered to the third person singular But exceptions have been made in respect of Chapter II, which is an account of our own work at the Institute, and of Chapter XIII, our concluding remarks In Chapter II our major findings about the foetal circulation are introduced by a description of the post-natal circulation, with which the reader is more familiar In addition, the older terms for certain parts of the foetal cardiovascular system are retained, even though we ourselves have long since discarded them as unsatisfactory The new terms, with the reasons for their introduction, are given in Chapter III and elsewhere, and a number of them are summarized in the glossary inserted between Chapters III and IV Until these new terms, or similar ones, are generally used, accounts of the foetal circulation and cardiovascular system will continue to suffer from the erroneous outlook of past centuries In some Schools the new terms are already in use,

di studiare il circolo fetale con metodo radiologico Inietta pertanto una sospensione di bario nella vena ombelicale e segue la sua diffusione mediante esami stereografici La scarsezza delle osservazioni non gli consente pero ancora di pronunciarsi decisamente su questo metodo We are indebted to Mr W J Bishop Sub Librarian of the Royal Society of Medicine for tracking down this note

[1] An important exception should be noted at this point So far as the adult is concerned we incline to the views of Pitts Magoun and Ranson (1939) rather than to those of Lumsden (1923 1924) in respect of the correlation of various types of respiratory pattern with the activities of definite respiratory centres But Pitts et al have not yet it seems extended their studies to the foetus and in the absence of such extension we have quoted though we do not necessarily subscribe to them views obtaining in the current foetal literature The passages in which these views are mentioned occur in sections (iv) and (v) of Chapter VI in section (ii) of Chapter VIII and in section (ii) of Chapter XI

[2] As Dr Barron has more or less simultaneously been producing a review (Barron 1944) and Sir Joseph Barcroft a book (still in preparation) on subjects which to some extent coincide with those of this present work we felt that it would be a great advantage if the three accounts gave independent valuations of the available evidence Though therefore we were privileged to see the draft of part of Sir Joseph s book we deliberately forgot what we had seen of Dr Barron s typescript we saw no part at all

and the teaching of the subject in these places is in consequence not only more in accord with the facts, but also simpler. We hope that other Schools will be equally ready to adopt the improvements which we have suggested, and thereby to share in the double advantage which we have mentioned.

The actual writing of the book was apportioned as follows: Dr Barclay and Miss Prichard undertook Chapter II and Dr Franklin the remainder. Personal communications from Sir Joseph Barcroft, and from Professors J Yule Bogue, J D Boyd, F J Cole, Clifford Formston, J A Gunn and Charles Singer, from Dr W F Harper and Dr G M Vevers, and from Mr M J Hirst and others are included by kind permission of these various friends and correspondents. Dr Douglas McKie, Editor of *Annals of Science*, generously allowed us to quote extensively from Vol 5 of his journal; Mr Tom Hopkinson, as Editor, and Mr Macdonald Hastings, as author, similarly permitted us to reproduce an account of lambing which appeared first in *Picture Post*. Many Librarians went out of their way to help us; we may mention in particular the Staff of the Radcliffe Library, Mr G F Home and Mr W J Bishop of the Royal Society of Medicine, the Librarian of the Royal College of Physicians of Edinburgh, and Dr Fred Bullock of the Royal College of Veterinary Surgeons. When the text was complete Professor Yule Bogue was kind enough to read through Chapter IV and to suggest certain improvements in it; we also benefited by his advice in respect of the final arrangement of Chapter VI. Sections (iii) and (iv) of Chapter VII are the gist of our comparative findings about the foetal liver; they owe much to a re-casting which our original account underwent at the hands of Professor A J E Cave, and we take this opportunity of expressing our very great indebtedness to him. We are also under a very deep obligation to Mr John Stallworthy, F R C S, who read through the part dealing with the human subject (Chapters IX to XII), suggested certain improvements in it, and—in its final form—gave it his imprimatur. Finally, in so far as the text is concerned, we are most grateful to Mrs J L Boldero, who very kindly undertook, as spare time work, practically the whole of the typing required.

In general the figures (apart from those already mentioned) were collected and arranged as follows: Dr Barclay and Miss Prichard dealt with the radiographs, including the five Plates; Dr Franklin and Miss Prichard with the rest. For figs 69–79 we wish to thank the Editor of *Picture Post* and Mr Kurt Hubschman; for figs 145–146 Drs C F V Smout and P Bacsich; and for fig 155 Dr J A Keen. The majority of the photographs[1] are the work of Mr M S Tuckey, technician at the Nuffield Institute, and his artistry in this line is obvious without further comment. For the actual preparation of the figs supplied by Dr Amoroso we are in large measure indebted to Mr R L Williams, F R M S, and Mr J Hancock of the Royal Veterinary College. Finally, in so far as the illustrations are concerned, we wish to thank the Editors and/or Publishers of the *Journal of Anatomy*, the *British Journal of Radiology* and the *Veterinary Journal* for permission to

[1] Many of them are halves of stereophotographs which can be viewed by those who care to pay us a visit. We have found stereophotography a most useful means of preserving records of foetal dissections; it often shows up details even better than do the actual specimens.

with our colleagues from Cambridge, and at the same time reduced our own opportunities for research In the intervals of other work, however, we have from time to time added to our experimental findings, and we have also made fairly extensive comparative anatomical studies

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reproduce various figures which appeared for the first time in those journals

Our long tale of acknowledgements may be completed by a mention of those who have assisted us, financially and otherwise, in the conduct of our experiments, or who have provided us with specimens Financial help, for which we were and are most grateful, came on more than one occasion from the Medical Research Council Personal help has been given by Drs E C Amoroso and J Badenoch, Professor J Yule Bogue, Drs J L Boldero, J G Emanuel and J D Little, Mr J C Scott, F R C S, Drs J Trueta and M Weatherall, Messrs D W H Barnes, G F M Carnegie, L T Cotton, R W Emanuel, J F Hale, N C Hughes Jones, H M Lloyd, D F Magee, R T Turner Warwick, and others, we wish to express to each of them our very sincere thanks For the provision of certain foetal and early post-natal specimens we are indebted to Colonel A E Hamerton and others of the Zoological Society of London, to Dr A H T Robb-Smith, and to Professor Charles O'Donoghue, to them also we offer similar thanks

The book which, with so much and so varied help, we have been able to produce contains the gist of seven years' radiographic, historical, and anatomical research upon the foetal circulation and cardiovascular system It is, therefore, too long and too detailed to make much appeal, except through its illustrations, to the dilettante reader We believe, however, that the more serious student will find himself amply repaid for a few days' careful perusal of our account, in view of the great interest inherent in its subject We trust, then, that our summary will be of service to medical and veterinary colleagues, to a fair proportion of medical and veterinary students, and to tutor-midwives, and we hope that, in return, they will adopt our simpler and more functional terms for certain parts of the foetal cardiovascular system Though we cannot at present forecast how much more we shall do in this particular field, we shall be grateful for any helpful comments on what we have written, for extra references, and for suggestions as to possible further lines of research It is, perhaps, unnecessary to add that all such help will be duly acknowledged in any future publications which we may make

With this preamble finished, we may pass on to the text proper, beginning with an account of the contributions made by our predecessors during the last eighteen hundred years

A E Barclay
K J Franklin
M M L Prichard

Oxford, 1944

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PART ONE

CHAPTER I

Historical Introduction, containing an Account of Earlier Views, based mainly upon Anatomical Findings, about the Course of the Foetal Blood Flow

THE history of research upon the foetal cardiovascular apparatus and the development of ideas about the foetal circulation can be divided into four parts. The first of these deals with the purely anatomical period that preceded Harvey's treatise (1628) on the blood circulation, the second with Harvey's own contribution, the third with the period of anatomy and of physiological hypothesis based mainly upon anatomy, and the fourth with the period of experimental research.

(i) THE PRE-HARVEIAN ANATOMICAL PERIOD

A detailed account, complete except for references to du Bois[1] (1555), du Laurens (1599), Bauhin (1600, 1605, 1620, 1621) and Spigel (1627), is already in print (Franklin, 1941, a, b), so a summary will suffice here.

In the second century A.D. Galen gave the first still extant description of the foramen ovale and its valve, and of the ductus arteriosus.[2] He also wrote briefly but tellingly of their post-natal closure.

In a posthumous publication, in 1555, Jacques du Bois mentioned membranous outgrowths (i.e. valves) in various veins, including the trunk of the vena cava as it passes forward from the liver. He thus, probably, anticipated Eustachi (1563), but his statement was so brief that one cannot say more than that.

In 1561 Gabriele Falloppio improved in one respect on Galen's account of the ductus arteriosus; he also initiated the special use of the word "placenta" (literally a flat cake or pancake).

In 1563 Bartolomeo Eustachi described and pictured the membrane that later became known as the Eustachian valve. Unfortunately, his figure of this structure was far from typical.

[1] Also referred to in the literature as Dubois and Sylvius. In this account the earlier writers are given their ordinary names rather than the Latinized versions of the same. Hence du Laurens (Dulaurens), Eustachi, Falloppio, Vesal, Aranzi, Botallo, Carcano, Fabrizi, Bauhin and Spigel rather than Laurentius, Eustachius, Falloppius, Vesalius, Arantius, Botallus, Carcanus, Fabricius, Bauhinus and Spigelius. But there are variants (e.g. Eustacchi, Gabrielle Falloppia, Fabritii, Fabrizio) of some of the above listed ordinary names, and the forms used here may not all be the best authenticated ones.

[2] Singer (1925, 20) wrote that Aristotle "perhaps has a reference—certainly the first in history—to the *ductus arteriosus*." According to Professor F. J. Cole (personal communication) D'Arcy Thompson's edition of the *Historia Animalium* 513a 35 footnote also gives this view, but in Professor Cole's opinion the identification is very far fetched and it is by no means certain that Aristotle knew of the pulmonary artery. According to Professor Singer (personal communication) Ogle in his edition of Aristotle's *On the Parts of Animals* held that Aristotle had a reference to the ductus arteriosus. Arthur Platt however did a very careful piece of work on the heart as described by Aristotle (see Singer's *Studies in the History and Method of Science* 2, 521) and concluded that Ogle was wrong.

In 1564 appeared the first account of the ductus venosus It occurred in a posthumous publication by Vesal, and the channel in question should be styled "Vesalii," and not "Arantii," if personal attributions are retained

In the same year Aranzi called the placenta the "uterine liver," and stated that the uterine vascular ramifications appeared to be separate from the umbilical ones

Leonardo Botallo, also in 1564, produced a short work in which he claimed to show the way, previously unknown, by which the blood passes from the right to the left side of the heart Actually, he described post-natal patency of the foramen ovale He never described the ductus arteriosus to which his name has been attached

Ten years later, Leone Giambattista Carcano published the first detailed account of the foramen ovale and ductus arteriosus

In 1599 du Laurens published the first figures of the foramen ovale and ductus arteriosus, but he did not adequately supervise the work, and the illustrations are the wrong way round, so they may well have confused those who had no personal acquaintance with dissections of foetuses In the third figure, also, the foramen ovale was placed between the opening of the coronary vein and the tricuspid valve of the heart

Girolamo Fabrizi d'Acquapendente, under whom Harvey studied for two years at Padua, published his *De formato foetu* at the beginning of the seventeenth century It contained descriptions and illustrations of the human placenta, umbilical vessels, ductus venosus, foramen ovale and its valve, and ductus arteriosus, it also included the results of wide comparative studies on lower animals, including the foetal lamb[1] Bertin (1753) particularly commended Fabrizi's appreciation of the vascular systems of the foetal liver

In 1605 Bauhin included, in his *Theatrum anatomicum,* a precis of what Eustachi had written on his membrane, in 1620 he reproduced Eustachi's figure of it But he stated, both in 1605 and in 1621, that he himself had never seen the structure

In 1626, in a posthumous publication, Spigel denied the existence of any direct communication between the uterine and umbilical arterial systems, he also noted that in the foetus the walls of the two ventricles are of equal thickness, whereas in the adult the left ventricle predominates In 1627 appeared his description, and Casserio's figure, of the "lobus exiguus" of the liver, it is what will be styled later in this book the "papillary process", the figure, as printed, was unintentionally a mirror-image or Spiegelbild! A collection of Casserio's anatomical plates, published independently in 1627, contained what was probably the first representation of the ligamentum arteriosum

(ii) WILLIAM HARVEY'S CONTRIBUTION

Harvey included in his treatise of 1628 the first account of the foetal circulation The relevant passages are to be found in Chapters VI, 33–6, XVI, 62,

[1] Since this was written Howard B Adelmann s superb edition of the embryological treatises of Fabrizi has appeared and has made these rather rare works more generally available in facsimile and translation The very full and scholarly annotations will also be of great help to present day readers

and XVII, 65-6 and are given in translation below, but they cannot be withdrawn from their context without some word of explanation

The first and longest passage occurs in the chapter in which Harvey treated of the routes by which the blood is carried from the vena cava into the arteries, or from the right ventricle of the heart into the left He began by pointing out that the connection of the heart with the lungs in the human being had resulted in much error in the absence of proper comparative studies on lower animals He then proceeded to describe the blood pathways from the venous to the arterial side in animals that have no lungs to complicate the story This led him quite naturally, to a description of the arrangements in the *foetuses* of animals that possess lungs, for he considered that these viscera are not functioning in utero as they are in post-natal life Harvey was, therefore, using the foetal circulation as an instance in support of his general argument and the passage should be read in this light

" Moreover " he wrote, " it has been borne in on me that the *same very* obviously holds good in the embryos of animals that have *lungs* For four cardiac vessels (namely, the vena cava the artery like vein [i e the pulmonary trunk] *the vein like* artery [i e the sinus of the pulmonary veins] and the aorta or great artery) are united in the foetus otherwise than in the adult, as is well known to anatomists

The first contact and union is that of the vena cava with *the vein like* artery This takes place a little above the *point* where the cava emerges from the liver and before it *opens into* the right ventricle, or gives off the coronary vein The union results in a lateral anastomosis that is a large free opening oval in shape perforating from the cava into the artery in question The opening is unimpeded hence blood can pass very freely and abundantly through it (as *through* a single vessel) from the vena cava into the vein like *artery and the left* atrium of *the heart*, and thence into *the left* ventricle Further, there is *in that* oval opening on the side facing the vein like artery a thin but strong membrane like a lid, which is larger than the opening Later on *in the adult* the membrane covers *over the* whole of this opening *and* fusing with it at all points, renders it quite impervious and well nigh effaces it *To revert* however to the foetus—this membrane is so arranged that, in falling back loosely on itself, it moves easily in the direction of the lungs and the heart and yields to the blood flowing *against it* from the cava but, on the other hand, prevents reflux of blood into that vessel Hence, one may justifiably consider that in the embryo the blood must continuously be passing through this opening from the vena cava into the vein like artery and thence into the *left* atrium of the heart On the other hand, once it has so *entered*, it can never flow back again

The other union is of the artery *like* vein (which occurs *after that* vein has left the right ventricle and is dividing into two branches) *It* is a sort of third trunk added *to these* two, an artery-like channel so to speak, leading obliquely *from* this point to the great artery and perforating into it Hence in the dissection *of* embryos there appear, so to speak, to be two aortae, or two roots of the great artery arising from the heart

"This channel, in the adult, narrows and dwindles in similar fashion to the foramen Finally, it dries up internally like the umbilical vein, and ceases to exist

"The artery-like channel in question has no membrane inside it acting as an obstacle to the blood-flow in either direction For there are at the mouth of the artery-like vein (of which, as I have said, the channel in question is an offshoot) three sigmoid valves facing from within outwards These yield easily to the blood flowing by this route from the right ventricle into the great artery, but completely prevent any reflux at all from the artery or from the lungs into the right ventricle, which they effectively shut off Hence, in this instance also it is proper to judge that in the embryo there is a continuous transference of blood by this route from the right ventricle into the great artery, during the contractions of the heart

"It is commonly said that these two unions, so large, free and open, have been made solely for the nutrition of the lungs, and that in the adult (though the lungs should now crave nutriment in greater amount because of their heat and movement) they cease to exist and are filled up This is an objectionable and inconsistent fabrication Equally false is the statement that in the embryo the heart is at rest, inactive and motionless, and that in consequence Nature was forced to make these passages for the maintenance of the lungs For one has only to look at an egg on which the hen has been sitting, and at embryos just removed from the uterus, to see quite clearly that the heart moves in them as in the adult, and that Nature is under no such compulsion I myself have often witnessed this movement, and the great Aristotle (Lib de Spiritu, cap IV) also testifies to it *The pulsation*, he says, *is evident from the very outset in the developing heart, as can be noticed in the dissection of living animals and in the growth of the chick from the egg* Further, we see these routes (both in man and in the other animals) open and free not only up to the time of birth (as Anatomists have described) but even after many months from birth, nay, in certain instances for a number of years, if not for the whole course of life, e g in the goose, snipe [?], and most birds, and in animals, particularly the smaller ones It was this, perhaps, that misled Botallo into thinking that he had discovered a new passage for the blood from the vena cava into the left ventricle of the heart, and I confess that my immediate reaction, on first finding this feature in a fairly large adult mouse, was somewhat similar

"These facts make it clear that there is absolute identity between what happens in the human embryo and what happens in others, in which the unions in question are not in process of abolition Hence the heart by its movement, transfers blood very freely from the vena cava, through both ventricular conduits, into the great artery The right ventricle receives blood from the atrium and then drives it forward through the artery-like vein, and its offshoot (the so-called artery-like channel), into the great artery The left ventricle, in like manner, simultaneously receives blood (that has been passed from the vena cava through the oval opening) by means of the atrial movement, and by its tension and contraction it drives this blood through the root of the aorta into the same great artery

"Thus in the embryo while the lungs are idle and devoid of activity or movement, as though they did not exist, Nature uses the two ventricles of the heart as one for the transmission of the blood And the condition of the embryo that has lungs but is not as yet making use of them, is similar to that of the animal that has no lungs at all

"The truth is thus as manifest in the foetus [as it is in the adult animal that has no lungs] namely, that the heart by its pulsation transports blood from the vena cava and discharges it into the great artery This it does by routes as free and open as would exist in man, if the intervening septum were removed and the cavities of the two ventricles communicated with one another

Having reached this point Harvey noted that, when the foetal unions become closed after birth in warm blooded animals, there is only one possible way by which the blood can pass from the right side of the heart to the left, and that is through the substance of the lungs He did not, however, go on to suggest in any detail why Nature should make this change, because a discussion of the physiology of respiration would have been foreign to the main purpose of his book Actually, it fell to the scientists working in Oxford later in the seventeenth century to demonstrate the function of the pulmonary blood circuit

In the second passage in the *Exercitatio* (XVI, 62) Harvey mentioned though not at any length the ductus venosus He had stated that the liver of the adult is interposed in the route of the blood from the intestines to the heart so that the chyle may have adequate time for its elaboration within the liver Otherwise it would reach the heart unchanged and have an adverse influence upon that organ

"In the embryo" he went on, "the liver has practically no function Hence, as one can see the umbilical vein passes intact through that viscus, and from the porta hepatis there is an opening or anastomosis, so that the blood returning from the intestines of the foetus (together with the maternal blood, and that returning from the placenta) makes for the heart, not through the liver but by the aforesaid umbilical vein The liver develops correspondingly later than the other parts in the earliest stages of foetal formation I have, indeed, seen all the members perfectly outlined in the human foetus and even the genitals distinct, while the liver was as yet merely rudimentary

In the third passage (XVII, 65-6), after pointing out the differences in structure and function between the right and left ventricles, Harvey continued

It is however to be noted that these matters are arranged otherwise in the embryo There is not the same difference between the ventricles, which are arranged almost equally, like twin kernels in a double nut The cone of the right ventricle reaches to the tip of the left ventricle so that the heart of the foetus is like a cone with two tips This is so (as I have already stated) because in the foetus the blood is not passing through the

"This channel, in the adult, narrows and dwindles in similar fashion to the foramen. Finally, it dries up internally like the umbilical vein, and ceases to exist.

"The artery-like channel in question has no membrane inside it acting as an obstacle to the blood-flow in either direction. For there are at the mouth of the artery-like vein (of which, as I have said, the channel in question is an offshoot) three sigmoid valves facing from within outwards. These yield easily to the blood flowing by this route from the right ventricle into the great artery, but completely prevent any reflux at all from the artery or from the lungs into the right ventricle, which they effectively shut off. Hence, in this instance also it is proper to judge that in the embryo there is a continuous transference of blood by this route from the right ventricle into the great artery, during the contractions of the heart.

"It is commonly said that these two unions, so large, free and open, have been made solely for the nutrition of the lungs; and that in the adult (though the lungs should now crave nutriment in greater amount because of their heat and movement) they cease to exist and are filled up. This is an objectionable and inconsistent fabrication. Equally false is the statement that in the embryo the heart is at rest, inactive and motionless, and that in consequence Nature was forced to make these passages for the maintenance of the lungs. For one has only to look at an egg on which the hen has been sitting, and at embryos just removed from the uterus, to see quite clearly that the heart moves in them as in the adult, and that Nature is under no such compulsion. I myself have often witnessed this movement, and the great Aristotle (Lib. de Spiritu, cap. IV) also testifies to it. *The pulsation*, he says, *is evident from the very outset in the developing heart, as can be noticed in the dissection of living animals and in the growth of the chick from the egg.* Further, we see these routes (both in man and in the other animals) open and free not only up to the time of birth (as Anatomists have described) but even after many months from birth, nay, in certain instances for a number of years, if not for the whole course of life, e.g. in the goose, snipe [?], and most birds, and in animals, particularly the smaller ones. It was this, perhaps, that misled Botallo into thinking that he had discovered a new passage for the blood from the vena cava into the left ventricle of the heart, and I confess that my immediate reaction, on first finding this feature in a fairly large adult mouse, was somewhat similar.

"These facts make it clear that there is absolute identity between what happens in the human embryo and what happens in others, in which the unions in question are not in process of abolition. Hence the heart, by its movement, transfers blood very freely from the vena cava, through both ventricular conduits, into the great artery. The right ventricle receives blood from the atrium and then drives it forward through the artery-like vein, and its offshoot (the so-called artery-like channel), into the great artery. The left ventricle, in like manner, simultaneously receives blood (that has been passed from the vena cava through the oval opening) by means of the atrial movement, and by its tension and contraction it drives this blood through the root of the aorta into the same great artery.

"Thus, in the embryo, while the lungs are idle and devoid of activity or movement, as though they did not exist, Nature uses the two ventricles of the heart as one for the transmission of the blood And the condition of the embryo that has lungs, but is not as yet making use of them, is similar to that of the animal that has no lungs at all

"The truth is thus as manifest in the foetus [as it is in the adult animal that has no lungs], namely that the heart by its pulsation transports blood *from* the vena cava and discharges it into the great artery This it does by routes as *free and* open as would exist in man, if the intervening septum were *removed* and the cavities of the two ventricles communicated with one another'

Having reached this point, Harvey noted that, when the foetal unions become closed after birth in warm blooded animals there is only one possible way by which the blood can pass from the right side of the heart to the left, and that is through the substance of the lungs He did not however, go on to suggest in any detail why Nature should make this change because a discussion of the physiology of respiration would have been foreign to the main purpo e of his book Actually, it fell to the scientists working in Oxford later in the seventeenth century to demonstrate the function of the pulmonary blood circuit

In the second passage in the *Exercitatio* (XVI, 62) Harvey mentioned though not at any length, the ductus venosus He had stated that the liver of the adult is interposed in the route of the blood from the intestines to the heart so that the chyle may have adequate time for its elaboration within the liver Otherwise it would reach the heart unchanged and have an adverse influence upon that organ

'In the embryo' he went on, 'the liver has practically no function Hence as one can see the umbilical vein passes intact through that viscus, and from the porta hepatis there is an opening or anastomosis, so that the blood returning from the intestines of the foetus (together with the maternal blood, and that returning from the placenta) makes for the heart, not through the liver but by the aforesaid umbilical vein The *liver* develops correspondingly later than the other parts in the earliest stages of foetal formation I have, indeed, seen all the members *perfectly outlined* in the human foetus and even the genitals distinct, while the liver was as yet merely rudimentary

In the third passage (XVII 65-6), after pointing out the differences in structure and function between *the right and left* ventricles, Harvey continued

It is, however, to be noted that these matters are arranged otherwise in the embryo There is not the same difference between the ventricles, which are arranged *almost equally*, like twin kernels in a double nut The cone of the right ventricle reaches to the tip of the left ventricle, so that the heart of the foetus is like a *cone with two tips* This is so (as I have already stated) because in the foetus *the blood* is not passing through the

lungs from the right ventricle to the left. On the contrary, these two chambers are equally busy with a single task (namely, the transference of blood from the vena cava to the great artery, though one does it through the foramen ovale, and the other through the artery-like passage, as I have already stated), and have identical parts to play in the distribution of the blood to the whole of the body. Hence the identity of their arrangements. When, however, it is time for the lungs to function and for the above-mentioned unions to be occluded, the ventricles begin to differ in strength and in the other respects that I have mentioned, because the right ventricle now drives the blood through the lungs only, but the left ventricle drives it through the whole of the body."

To complete the story as given by Harvey, one must mention a further passage that is to be found in the second of his *Exercitationes*, addressed in 1649 to Riolan the younger. In this passage he stated that the blood moves through the lungs only when these are moved in the act of respiration, and not when they are collapsed and quiescent. This was probably, he went on, the reason why Nature had instituted the foramen ovale in the foetus.

If one analyses Harvey's contribution, one finds first that he integrated the best passages in previous *anatomical* accounts of the foramen ovale and ductus arteriosus though he did not, as one would to-day, publicly acknowledge his sources. To the knowledge thus integrated, he himself added relatively little. In fact, one may say that his chief contribution was his emphasis on the intra-uterine size of the ductus arteriosus, which he likened to a twin-root of the great artery (i.e. of the aorta distal to the point at which the ductus joins it). If he was, as seems possible, responsible for the introduction of the term "foramen ovale," then this was his second contribution of importance. To the anatomical data that he had synthesized, he added his revolutionary *physiological* discovery that the blood circulates, and that at considerable speed, from the heart to the arteries, and from the veins back to the heart.

Harvey's chief merit, then, was that he introduced the dynamic concept of a vigorous circular movement of the blood. The chief error in his account was his denial of a pulmonary circulation in the foetus. It is not possible to say on what he based this denial; actually, as one now knows, the pulmonary blood flow in the mature foetus is both considerable and rapid (Barclay et al., 1942, *J. Physiol.*). A more general criticism is applicable not only to Harvey's description of the foetal circulation, but also to all subsequent ones that were produced before Pohlman (1907) inaugurated the modern phase. This criticism is that the descriptions were based not upon direct experimental findings, but merely upon more or less correctly determined anatomical data, supplemented in some cases, but certainly not in all, by experience of living foetuses other than human ones. Upon such bases successive writers built up successive working hypotheses of the foetal circulation, but they remained hypotheses, and the degree to which they were accepted depended not upon their approximation to the truth, for there was no way of testing this in the absence of experimental work, but—as will be seen in the subsequent story—upon purely accidental circumstances.

A more special criticism could be directed against Harvey's account had his description of the foetal circulation been more than an incidental illustration in support of a general argument not directly concerned with foetal matters This criticism is that he followed his predecessors, who had not the benefit of his views upon the blood movement, and, by concentrating his attention on the foramen ovale instead of on the posterior caval channel he missed one of the main features in the foetal cardiovascular system, namely, the bifurcation of that channel into left and right terminal divisions Had he disregarded previous accounts and mentally followed the blood in its course up the posterior vena cava, he could hardly have failed to notice the true orientation of the parts As it was, one and a half centuries elapsed before the correct view was first published (Wolff, 1776), and even then it failed to be appreciated by more than a few, indeed, it has only very recently gained wider acceptance (Amoroso et al, 1942)

One thing that Harvey definitely did not write was that the blood from the two venae cavae mixed in the right atrium and that thereafter part of the mixture went via the foramen ovale into the left atrium Who first so misread Harvey's statements it is not easy to determine But the persistence into modern times of such misrepresentation is undoubtedly due to Kilian (1826) and to Knabbe (1834) for the latter's account was passed on by Preyer to Ziegenspeck and thereby reached Pohlman (1909), whose statement on the matter was accepted by Kellogg (1928)

(iii) THE PERIOD OF ANATOMY AND OF PHYSIOLOGICAL HYPOTHESES BASED MAINLY UPON ANATOMY 1628–1907[1]

One of the interesting points about Harvey s account of the foetal circulation is that he made no reference in it to Eustachi s membrane In 1649 Riolan the younger stated that it was impossible to decide what Eustachi had meant at the same time, it is clear that Riolan himself was familiar with a reticular membrane at the threshold of the atrium '

In 1651 Harvey emphasized, as Aranzi had done in the previous century, the separateness of the maternal and foetal cardiovascular systems

In the same year, his friend Highmore gave an explanation of the postnatal closures of the caval opening (i e of the foramen ovale) and the ductus arteriosus, in some ways it has a fairly modern ring The closures, in Highmore s view were connected with the onset of respiration, which diverted into the lung vessels the blood that previously flowed through the two foetal channels and thence into the aorta The ductus in consequence collapsed, and the pulmonary venous return apposed the membrane over the caval opening Highmore did not merely fail like his friend Harvey, to mention Eustachi s membrane but stated very definitely that there are no valves in the vena cava

[1] The complete story from 1628 to modern times is still in course of preparation for the literature to be read is very considerable and many of the books that would normally be available are not so in war time When the full account has been written it will be offered for publication in *Annals of Science* Meanwhile this preliminary sketch will at least indicate the more important advances of the last three hundred years

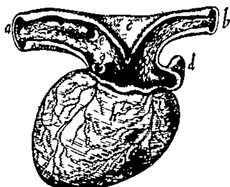


FIG 1 —From Lower (1669) Plate II fig 2 The intervenous tubercle of a quadruped (such as the sheep dog horse or ox) displayed by opening up the vena cava and right atrium *a* The trunk of the ascending [posterior] vena cava *b* The trunk of the descending [anterior] vena cava *c* The swelling separating the two veins *d* The right atrium *e* The foramen ovale *g* The coronary vein [sinus] *h* The heart [i e the ventricles]

Between 1652 and 1656 the structure in question was rediscovered by Charles le Noble, and a colleague, Guiffart, named it "valvula nobilis," partly in honour of le Noble, partly because it was itself worthy of the epithet in question

In 1656 Domenico de Marchettis made the first mention of the bronchial arteries and veins, though the actual name "bronchial" was coined nine years later by Ruysch In 1661 Malpighi produced the first descriptions of capillaries and of the terminal air-spaces in the lungs About this time, a group of Oxford scientists had begun to demonstrate the changes that occur within the blood during its passage through the lungs In 1660 Robert Boyle took the first step by showing that part of the air is essential to life, and in 1667 Hooke proved that respiration depends on an adequate supply of fresh air to the lungs In the same year Walter Needham called the placenta the "uterine lung" In 1668 Hooke postulated that dark blood becomes florid on passing through the lungs because it mixes with the air, Lower (1669) experimentally verified Hooke's postulate and also showed that venous blood owes its dark colour to loss of air It is still not easy to assess the position of John Mayow in respect of original research He did, however, publicize with some skill the results of the Oxford workers, even if he did not adequately acknowledge his sources, and in his second book (*Tractatus quinque*, 1674) he stressed the need of the foetus for a sufficient supply of nitro-aerial particles or, as one would now say, of oxygen In the adult these particles entered the blood via the lungs, in the foetus they must enter it during its circuit, within the umbilical vessels, through the placenta or uterine caruncula

Lower's contribution to respiratory physiology has been noted In the same treatise (1669) he described the intervenous tubercle or swelling (fig 1) and gave an account of the foetal circulation The passage about the tubercle may be translated as follows "Just before the threshold of the right atrium, that is to say, where the ascending vena cava joins the descending and prepares to discharge into the atrium of the heart, a certain small swelling is formed by underlying fatty tissue This swelling is well worth attention Its interposition at this point causes the blood, which falls down the descending vein, to be diverted into the atrium, when it would otherwise have continued on down into the ascending vein and have caused great hindrance and slowing to the blood flow up through that vein into the heart" Lower thought that the swelling was more pronounced in man than in lower animals and he so depicted it One may state at once that this view has not since found much support But the tubercle is of considerable importance to the foetal circulation in certain animals, and Lower himself brought it into his account of that circulation

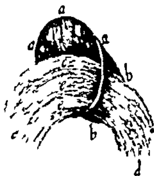


FIG 2.—From Lower (1669), Plate II, fig 3. *aaa* The edge of the foramen ovale to which the membrane [valve] is attached. *bb* The same membrane hanging down below the circumference of the foramen. *c* The blood flowing along in the vena cava. *d* Where this blood flows into the pulmonary vein [left atrium]. *eee* Where it drives back the membrane and rushes on through an open door.

Various comments can be made about that account. The first is that Lower accepted some degree of pulmonary blood flow during foetal life. The second is that for him the foramen ovale was presumably a by-pass for *inferior* caval blood only. For the foramen lay in the ascending vena cava below (i.e. caudal to) the tubercle, and the function of that tubercle was to keep the superior caval blood away from the inferior caval blood. If, however, one concedes this, one must point out the omission of the word "inferior" before "vena cava" in his next sentence which reads, "Through this foramen the greater part of the blood returning in the vena cava passes ... across into the pulmonary vein [i.e. the left atrium]." The deduction about the omission is supported by the figure (fig 2) of the blood flow through the foramen, for by no stretch of the imagination can the pathway *c* to *eee* be taken to represent a superior caval flow, when that from *eee* to *d* represents the flow from the foramen towards the left ventricle.

Lower, like Harvey and Highmore, made no mention of Eustachi's membrane, or Riolan's membrane, or the valvula nobilis. But in 1682 the last-named was reported to have been found in a beaver dissected together with a number of other animals under the directions of the Royal Academy of Sciences of Paris. As the valve is absent from many animals, this first mention of its occurrence outside human subjects is of interest. The description, translated by Pitfeild, was published in England in 1688 and 1702, and read as follows: "Under the *Vena coronaria* we found the *Valve* called *Noble* which fills the whole Trunck of the *Vena Cava*, and which was so disposed, that the Blood might easily be carried from the *Liver* to the *Heart* by the *Vena Cava*, but which is hindred from descending from the *Heart* towards the *Liver* through the same Vein."

Between 1693 and 1722 Jean Mery, a Paris surgeon and anatomist, advanced and maintained the view that blood passed from left to right through the *foramen ovale*. Though his publications and his disputes with du Verney and others cannot be passed over in a complete account, they are too long to summarize here, and it must suffice to say that they retarded rather than advanced progress. Verheyen (1710), by contrast, was very modern in outlook.

In 1702 William Cowper wrote of a 'peculiar valve' that he had lately discovered in the inferior vena cava near the right atrium. His figures were published posthumously in 1724, and included one of the valve in a man nearly eighty years of age. In 1707 Boerhaave brought out a new edition of Eustachi's *Opuscula anatomica* in which, as noted earlier, the valve had first been described and depicted. Six years later again Douglas published, in Cheselden's *The Anatomy of the Humane Body*, a figure of the human diaphragm and thoracic inferior vena cava viewed from the cranial aspect

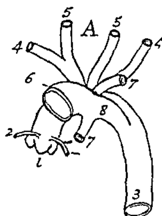


Fig 3—Copied from Cheselden (1713) Table XXIII *A* The great Vessels in the *Thorax* of a *Fœtus* fill'd with Wax 1 The beginning of the *Aorta* 2 The Coronary Arteries of the Heart 3 The Descending *Aorta* 4 The Subclavian Arteries 5 The Carotid Arteries 6 The Pulmonary Artery a piece of it being cut away to bring the Beginning of the *Aorta* in sight 7 The Branches of the Pulmonary Artery going to the Lungs 8 The *Ductus Arteriosus* running directly from the Pulmonary Artery into the *Aorta*

The sternal half of the lumen of the vein was occupied by "The *Valvula nobilis* of the *Cava ascendens*," but no mention was made of the structure in the text of the book

By 1714, then, four anatomists had independently discovered the membrane or valve, and it had been described and pictured with varying success in a number of books On the other hand, its presence was perhaps not very generally recognized, it had several aliases, and suggestions as to its function were largely wanting It was in this year that Lancisi published, with comments, the recently discovered *Tabulæ Anatomicæ* of Eustachi, in which the figure of the membrane appeared twice (Pl VIII, fig 6, and Pl XVI, fig 3) The legend provided by Lancisi for the second plate contained a suggestion as to the function of the valve "Further," he wrote, "we consider as specially noteworthy two valves The larger of these [i e the Eustachian valve] was demonstrated by Eustachi a century before Lower [published his account of the intervenous tubercle] Its function is, presumably, to prevent the jugular blood, coming down *through the superior vena cava, from colliding too* violently with the blood coming up through the inferior vena cava" In other words, Lancisi adopted for the valve a use similar to that which Lower had suggested for his tubercle

In 1715 Vieussens described and pictured the "isthmus" surrounding the "fossa of the vena cava" (fossa ovalis) It was not his first mention of this *feature but it was the first mention of it under the new name According to* him, its generally accepted function was to ensure that the superior caval blood did not oppose the movement of the inferior caval blood and render it difficult for the latter to enter into the right atrium and ventricle Vieussens' whole outlook, so far as the cardiovascular system was concerned, was unscientific, so one need not give his views on the foramen ovale

In 1717, in a dissertation that he sent to Morgagni, Lancisi again wrote of the Eustachian valve *What he said may be somewhat freely translated* as follows "In us, who stand and walk upright, the superior caval blood descends more readily and rapidly to the heart through its own weight—especially in exercise—than the inferior caval blood ascends to the heart To divide and blunt the remaining force of the descending blood (already reduced by the almost horizontally directed azygos inflow), there is provided in the inferior vena cava near the atrium of the heart a sort of valve, as pointed out by Eustachi *This valve is not found in pronograde animals*" This comparison of the findings in man and in lower animals was a considerable contribution, even if Lancisi's conclusion is not universally true

In the same year, 1717, Winslow delivered to the Royal Academy of Sciences

his first memoir on the valve He had been stimulated to look for the structure through reading the brief note of Jacques du Bois (1555) Winslow failed to find any such valve in the sheep but he did finally discover it in human subjects He described it as ' une Valvule tres considerable, d une grande beaute, en partie membraneuse, & en partie en forme de rezeau" Because he had recently seen Lancisi's edition of the Plates of Eustachi, Winslow generously named his finding the reticular valve of Eustachi

The variability shown by the valve had led him to further research, and he reported his findings as follows

(1) It is vestigial in the adult

(2) It is often present, though in varying degree in young subjects

(3) When it is incomplete it is the reticular part that is the more deficient

(4) The valve is found complete in very small infants, much reduced in older ones

(5) The diminution appears to be proportional to that of the foramen ovale and the disappearance to the closure of the foramen When the valve is found in adults the foramen ovale is persistent

These results led him to suspect that the valve had some relation to the foetal circulation and that its chief function must be in connection with that circulation He suggested that it not only diverted the superior caval stream from the inferior caval one, as advanced by Lancisi, but also prevented superior caval and coronary blood and reflux via the foramen ovale from passing back into the inferior vena cava

Du Verney had been unable to attend Winslow's demonstration, but in the summer of 1717 he invited Winslow to examine with him twenty one subjects that showed the valve (Winslow, 1725) The findings were opposed to Winslow s previous ones for it was obvious that the valve might persist without reference to age or to the continued patency of the foramen ovale

According to Haller (1763 26) the valve began to be more generally known after the appearance of Winslow's *memoirs* (1717, 1725) Certainly, there was soon a veritable spate of publications about it It is impossible to refer here to all of these but one can at least mention one or two of the accounts

In 1728 Lancisi again attacked Lower, apparently in the belief that he had, so to speak stolen Eustachi s membrane and turned it into his intervenous tubercle the accusation one need not add, was quite unjustified Lancisi also went into fuller detail about the valve and said that in pronograde animals its place was taken by a semicircular muscle

Eight years later Trew produced a very fully illustrated book upon the differences between the human being before birth and the human being after birth It is well worth attention not only in respect of the Eustachian valve, but also in connection with the more particularly foetal parts of the cardiovascular system (see e g fig 4) Trew said that the valve is found both in the foetus and in the adult, in the latter it may be proportionately as large as other parts that persist after birth, and it can be present although the foramen ovale is closed Both before and after birth, he thought, it prevents reflux of blood into the inferior vena cava during atrial systole, in the foetus, in addition, it serves to direct the inferior caval blood towards the

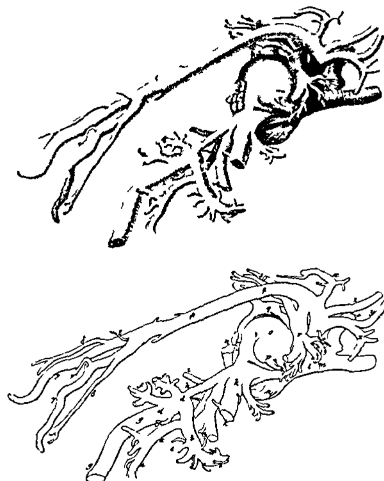


FIG 4—From *A Compleat System of the Blood Vessels and Nerves* etc London 1750 Plate II fig 24 It is actually an improved copy of Trew (1736) Plate II fig 23 and gives a right latero dorsal and somewhat caudal view of the greater part of the cardiovascular system of a human foetus The 1750 legend is as follows *a a* The vena portarum running across the liver *b c d* The sinus of the vena portarum the right portion of which *b* distributes its branches *e e e e* through the greater or right lobe of the liver but *the left one c goes to the lesser or left lobe At its entry it is enlarged* into *d d* and sends off the branches *f f f f* Below it receives the umbilical vein *g g* and above it sends off the canalis venosus *h* which below the branches of the vena cava *i i i i i* collected from each lobe of the liver is joined to the trunk of the inferior or ascending vena cava *k k* with which is united the trunk of the superior or descending vena cava *l* composed of the two jugulars ** and the vena azygos or sine pari *m* both which trunks form the right auricle *n* *o* The sack *of the left auricle into which enter* the branches of the right pulmonary vein *p* and of the left *q* *r* The right branch of the pulmonary artery *s s* The left *t* The canalis arteriosus arising from the pulmonary artery near its bifurcation and united with the arch of the aorta *z z* *x* The right subclavian *y The right carotid* *z The left carotid* *α* The left subclavian *β* The descending aorta divided at the iliac region on each side into *γ γ* The umbilical artery and *δ δ* The crural *ε* The arteria sacra sent off at the division of the aorta

foramen ovale He did not include in its functions the separation of the superior and inferior caval streams

Senac, in his notable treatise on the heart (1749), also considered that the valve served to direct the inferior caval blood to the foramen ovale It would be quite impossible to summarize here the long survey that Senac gave of past work upon the fœtal cardiovascular system and circulation, one can only recommend its careful perusal to those readers who wish for fuller details

Lieutaud (1754) said that the Eustachian valve was normally present in the foetus, *often in children*, and sometimes in the adult He called it "digue membraneuse" because, in his view, it was not analogous to the valves found in veins, despite the epithet "membraneuse," he realized that there may be muscle fibres between the two membranous layers He spoke of its function *only in so far as the foetus* is concerned By prolonging the inferior vena cava, it deepens the lower part of the right atrial cavity, and it directs the blood, as Senac noted, *towards the foramen ovale*

In the year previous to Lieutaud's communication, Bertin revived interest *in a part of the foetal* cardiovascular system that had for long been comparatively neglected namely, the liver Aided by coloured wax injections, he had re-investigated the venous

arrangements in the liver of the human foetus, and had found that the umbilical and portal branches were mainly in the lower, concave portion of the organ while the hepatic branches of the vena cava were in the upper, convex portion The portal vein does not form a sinus as it does in the adult, it does not even have a left branch The left lobe of the liver is supplied by branches from the umbilical vein only the right lobe by branches common to the umbilical and portal veins (fig 5)

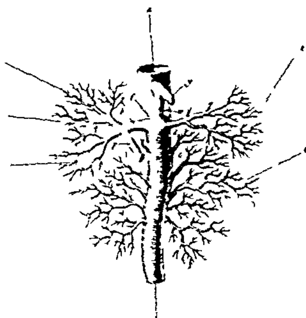


Fig 5 —From Bertin (1753) Human foetus The umbilical vein *uu* gives off minor left *eee* and right *ii* branches and then the largest left *d* and right *o* branches The ductus venosus *ic* passes from the umbilical vein to be inserted into the left hepatic vein *s* which joins the inferior vena cava *a* The branches *qq* supplying the right lobe of the liver carry mixed umbilical blood coming through *b* and portal blood coming through *p* the trunk of the portal vein

The portal flow is small by comparison with the umbilical if one may judge from the relative sizes of the two vessels Hence, in the foetus the left lobe of the liver is very distended and as large as the right lobe Incidentally, the whole organ is extremely large and reaches down to the iliac crest

After birth with the cessation of the umbilical flow and the occlusion of the umbilical vein ductus venosus and certain intra hepatic branches of the umbilical vein the portal flow passes through all the remaining vessels of the umbilical portal system and the portal sinus of the adult develops, while the liver as a whole assumes gradually its definite and characteristic shape, though this process requires some years for its completion

How far Bertin s work became known and accepted it is not easy to assess, but a score of years later Sabatier considered that there was little or nothing to add to the story and there is no doubt that it was a major contribution to knowledge of the foetal liver

No large branch of anatomy or physiology was overlooked by Albrecht von Haller and he not only added to, but also summarized, knowledge about the foetal cardiovascular system and views about the foetal circulation So early as 1737 he produced a work on the Eustachian valve and other publications followed at intervals, he also encouraged the efforts of many other writers For brevity's sake, however reference will be made here only to his *Opera minora* 1763 and to his *Elementa physiologiae corporis humani*, 1757-66

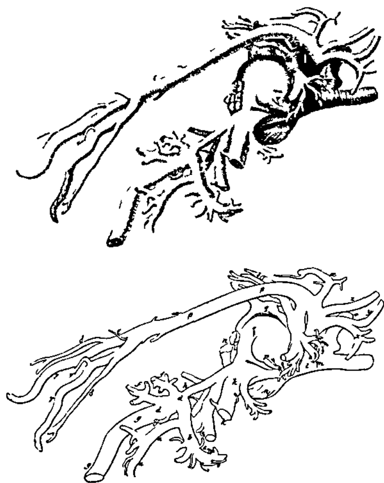


FIG 4 —From *A Compleat System of the Blood Vessels and Nerves* etc London 1750 Plate II fig 24 It is actually an improved copy of Trew (1736) Plate II fig 23 and gives a right latero dorsal and somewhat caudal view of the greater part of the cardiovascular system of a human foetus The 1750 legend is as follows *a a* The vena portarum running across the liver *b c d* The sinus of the vena portarum the right portion of which *b* distributes its branche *e e e e* through the greater or right lobe of the liver but the left one *c* goes to the lesser or left lobe At its entry it is enlarged into *d d* and sends off the branches *f f f f* Below it receives the umbilical vein *g g* and above it sends off the canalis venosus *h* which below the branches of the vena cava *i i i i i* collected from each lobe of the liver is joined to the trunk of the inferior or ascending vena cava *k k* with which is united the trunk of the superior or descending vena cava *l* composed of the two jugulars ** and the vena azygos or sine pari *m* both which trunks form the right auricle *n* *o* The sack of the left auricle into which enter the branches of the right pulmonary vein *p* and of the left *q* *r* The right branch of the pulmonary artery *s s* The left *t* The canalis arteriosus arising from the pulmonary artery near it s *bifurcation* and united with the arch of the aorta *v v* *x* The right subclavian *y* The right carotid *z* The left carotid *α* The left subclavian *β* The descending aorta divided at the iliac region on each side into *γ γ* The umbilical artery and *δ δ* The crural *ε* The arteria sacra sent off at the division of the aorta

foramen ovale He did not include in its functions the separation of the superior and inferior caval streams

Senac, in his notable treatise on the heart (1749), also considered that the valve served to direct the inferior caval blood to the *foramen ovale* It would be quite impossible to summarize here the long survey that Senac gave of past work upon the fœtal cardiovascular system and circulation, one can only recommend its careful perusal to those readers who wish for fuller details

Lieutaud (1754) said that the Eustachian valve was normally present in the foetus, often in children, and sometimes in the adult He called it "digue membraneuse" because, in his view, it was not analogous to the valves found in veins, despite the epithet "membraneuse," he realized that there may be muscle fibres between the two membranous layers He spoke of its function only in so far as the foetus is concerned By prolonging the inferior vena cava, it deepens the lower part of the right atrial cavity, and it directs the blood, as Senac noted, towards the foramen ovale

In the year previous to Lieutaud's communication, Bertin revived interest in a part of the foetal cardiovascular system that had for long been comparatively neglected, namely, the liver Aided by coloured wax injections, he had re-investigated the venous

atrium and in the adult it prevents reflux of blood from that atrium, during its systole, into the inferior vena cava It probably does not have the function assigned to it by Lancisi Its function in the foetus is described below

Haller's description of the foetal cardiovascular unions may be omitted from a brief survey such as the present one, his account of the foetal circulation on the other hand, should be reproduced at some length It is given in sections in Vol VIII, and may be rendered in somewhat abbreviated form, as follows

'The greater part of the foetal blood passes from the iliac into the umbilical arteries and is carried in these latter to the placenta This as I have pointed out, is the reason for the small size of the foetal pelvis and lower limbs The blood returning from the placenta is increased by the nutrient fluid sent by the mother to the foetus It passes into the umbilical vein, which sends a small part perhaps a seventh of its blood direct into the vena cava, below the diaphragm it is true, but very close to the heart The remaining six sevenths of the blood returning from the placenta pass into the liver through vessels that in the foetus are offshoots of the umbilical vein but in the adult are offshoots of the portal vein After the blood has been dispersed through the liver, it is collected again in the hepatic branches of the vena cava and, uniting with the blood of the ductus venosus passes through the diaphragm to the nearby right atrium Here the Eustachian valve prevents it from going to the right ventricle, in consequence, it must keep straight on and in great part, make for the foramen ovale There it exerts pressure upon the valve and pushes its free upper portion away from the isthmus towards the left atrium where there can be no corresponding force to oppose it The blood thus opens a way for itself so that as large a part of it as the valve movement will allow passes upwards and backwards from the right atrium to the left atrium This is the route that is followed by air or fluid injected into the umbilical vein or the inferior vena cava It stands to reason that the inflow into the left atrium occurs during the diastole and not during the systole, of the atria From the left atrium the blood goes to the left ventricle and thence into the aorta

'The portion of the umbilical vein blood that could not pass through the foramen ovale as also that part of the blood that returns from the head and upper limbs via the superior vena cava passes to the right ventricle and thence into the pulmonary artery [trunk] A minor portion only goes to the lungs the major portion passes via the ductus arteriosus to the descending aorta The aortic trunk before it is joined by the ductus, is narrower than the ductus and the blood received by the aorta via the ductus is almost more than it receives from the left ventricle As a considerable portion of the umbilical vein blood passes by this route the wider the ductus is the more will the lower parts of the body increase in size'

The above is a remarkable account when one considers the material from which Haller had to construct it But, near to the truth as it came, it could

The former contained the final versions of two works on the Eustachian valve, namely, the one already mentioned and another that was first published in 1748 In the first of these Haller stated that he had examined thirteen cadavers, that no completely satisfactory picture of the valve was available (his own later ones are open to similar criticism), and that the descriptions of it were themselves somewhat obscure He styled it the Eustachian valve of the vena cava It was *always present in the [human] foetus*, and he had also found it in every adult subject that he had examined, though the oldest of these subjects had been over eighty at death From a study of Trew's figures, however, he judged that the valve was relatively wider in the foetus In the past descriptions had in some cases been confused, and Haller felt it necessary to state that the valve could readily be distinguished from the isthmus of Vieussens on the one hand, and from the tubercle of Lower on the other Incidentally, Haller disbelieved in the existence of the tubercle

With regard to the physiology of the valve, he wrote "There is doubtless some function for this elegant structure, but we do not yet fully know what is that function " He then went on to give what was in effect a summary of previous views, including the suggestion that in foetal life the valve directs the inferior caval blood towards the foramen ovale

The second memoir contained a number of figures of the valve, but they were not very good ones, and the main interest of the work lies in the foot-notes, which contain details about many parts of the foetal cardiovascular system In some of these notes there is a hint of Haller's embryological studies Like Mery and others before him, Haller measured the lumina of various foetal blood vessels and channels The measurements themselves are of interest (e g he found that in the early foetus the ductus arteriosus by itself, and in the mature foetus the pulmonary trunk, exceeded in calibre the aorta), but one must note that such quantitative data have more than once led to incorrect estimates of the amounts of blood flowing through the various channels, these estimates being based on the assumption that the blood flow varies as the cross-section of the vessel through which it passes Other parts of the treatise dealt with the Thebesian valve, the foramen ovale and its valve, the ductus arteriosus, the post-natal closure of the two channels, the fossa ovalis, and the isthmus of Vieussens It is not possible to summarize Haller's statements about all these , with regard to the isthmus, however, one may note that he was dissatisfied with Vieussens' term, and himself proposed, as a better but still not ideal alternative, the name "annulus fossae ovalis "

In his *Elementa physiologiae corporis humani* Haller again showed his remarkable gift of synthesizing an already vast literature So far as the foetal cardiovascular system and circulation were concerned, the important passages appeared in Vols I (1757), VI (1764), and VIII (1766) In these passages he dealt with the tubercle of Lower, the Eustachian valve, the ductus venosus, the foramen ovale, the ductus arteriosus, and the foetal circulation

As already noted, he disbelieved in the existence of the tubercle The Eustachian valve, he said, when most complete (as it commonly is in the foetus), shows no reticulation, which is a form of degeneration in this and other valves The valve is not peculiar to the foetus It completes the wall of the right

left ventricle and after that into the aorta and its upper branches, namely, the axillary and carotid arteries It returns via the superior vena cava to the right atrium and is driven thence into the right ventricle and pulmonary artery ' Some of the blood from this vessel circulates through the lungs and in the left atrium mixes with the blood from the inferior vena cava The rest passes on some of it to supply the lower parts of the body some to enter the umbilical cord In this way the best and quasi arterial blood goes to the thymus and brain and that which returns to the placenta is derived solely from exhausted venous blood

Nicholls concept was followed by one that bore some resemblance to it but which was destined to become far better known and indeed to remain for a century and a half with minor modifications the dominant hypothesis of the foetal circulation Because of this it must be described at greater length than its intrinsic merit perhaps demands It is to be found in a memoir by Sabatier that was included in *Histoire de L'Academie Royale des Sciences*, 1774 but was not actually published until 1778 Sabatier dealt first with the foetal blood circulatory organs excepting the umbilical vein and ductus venosus, which he considered had been adequately described by Bertin in 1753

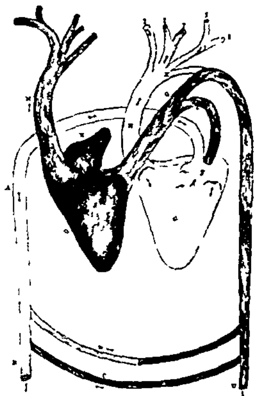


Fig 8—From Nicholls (1773) Plate XI To illustrate his concept of the foetal circulation (see text) *A* inferior vena cava which carries blood from *B* the umbilical vein *D* the liver and *C* the lower parts of the foetus to the heart The blood is discharged through *E* the foramen ovale into *F* the left atrium From the atrium it is forced into *G* the left ventricle and thence into the axillary and carotid arteries It returns through *M* the superior vena cava to *N* the right atrium and is forced into *O* the right ventricle whence it reaches *P* the pulmonary artery Part of it then goes through the lung arteries to the left atrium to be mixed with the inferior caval blood part goes through *Q* to *RST* the lower parts of the body and to *U* the umbilical cord

He began with the Eustachian valve first accurately described by Winslow (1717) Winslow he said had been wrong in the functions he suggested for this valve for

(1) The valve of the foramen ovale prevents reflux from the left atrium to the right atrium hence the blood of the two chambers cannot mix

(2) Blood cannot pass back to the umbilical vein when the only direct communication between the right atrium and that vein is through the very narrow ductus venosus scarcely capable of transmitting one-sixth of the blood from the placenta

carry no more conviction than Haller's personal authority gave to it, and there was nothing to prevent other concepts being advanced The first one that needs to be noted was that put forward by Nicholls in 1773, it appeared in his *Disquisitio de motu sanguinis et cordis in homine nato et non nato* Some of the physiological ideas expressed in the text were strange products, and the main interest of the book is undoubtedly in its illustrations and their legends Some figures copied from Trew, and some original ones, depict various parts of the foetal cardiovascular system, while one plate shows Nicholls' idea of the foetal circulation His *Pl VIII, fig* 3, is of the opened right atrium of a foetus, and it shows the "valvula nobilis interposed between the atria of the heart The valve is proportionately larger in the foetus than in the adult" His *Pl IX* contains an interesting dorsal view of a foetal heart, with the valvula nobilis and the foramen ovale and its valve, exposed by removal of parts of the atria and vessels (fig 6) His *Pl X* (fig 7) is a diagram in which the arch of the aorta diminishes in calibre as it gives off its branches until only a very narrow "channel of communication" remains to unite with the "pulmonary artery" [i e the pulmonary trunk and ductus arteriosus] which, after giving off branches [i e the pulmonary arteries] to the lungs, is continued as the descending aorta Nicholls obviously regarded the left ventricle of the foetus as supplying the head and upper extremities, and the right ventricle as supplying the rest of the body, the flow through the "channel of communication" being negligible His *Pl XI*, finally, is a diagram showing his concept of the foetal circulation (fig 8) The inferior caval blood, derived from the umbilical vein, liver and lower parts, passes through the foramen ovale to the left atrium, whence it is driven into the

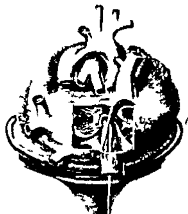


FIG 6—*From Nicholls (1773)* part of Plate IX Dried heart of *a human foetus dorsal aspect* Parts of the walls of the atria have been removed to show the Eustachian valve and the foramen ovale The probe passes up through the inferior vena cava and foramen ovale into the left atrium The superior vena cava the pulmonary arteries and veins the aorta and its branches and the ductus arteriosus are all recognizable without further explanation Note *the narrowing of the aortic arch* before its union with the ductus arteriosus References in the text to Nicholls plates are shown in italic

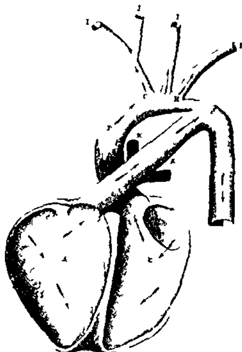


FIG 7—*From Nicholls (1773) Plate X* *A* right ventricle receiving blood from the right atrium *B* pulmonary artery which gives off branches *KK* to the lungs and then goes on to form the whole of *D* the descending aorta *HC* the channel of communication which passes from the aortic arch *to the end of the ductus arteriosus* *E* the left ventricle from which arises the trunk *FG* of the aorta which gives off the axillary and carotid arteries

blood collected by the superior vena cava from all the parts supplied by the carotid and subclavian arteries, so that this blood may be returned by the umbilical arteries to the placenta and there have its vitality restored before returning to the foetus by the umbilical vein Thus the course of the circulation is somewhat like a figure of 8 The umbilical vein which collects the blood from the placenta discharges it into the inferior vena cava either by the ductus venosus or else by the hepatic veins after a passage through the substance of the liver It then goes through the foramen ovale to the left atrium and ventricle The three large branches arising from the upper part of the aortic arch next carry it in large measure to the head and upper extremities It returns to the heart by the superior vena cava, and passes through the right atrium and ventricle into the ductus arteriosus once again

This simple mechanism known Sabatier believed to no one but himself, provides that blood that has circulated through the placenta shall return to that organ only after it has passed through all parts of the foetus, a great improvement on the generally accepted schema

The union of the pulmonary trunk and of the aorta serves yet another useful purpose For the blood expelled into the descending aorta by the action of both ventricles flows thereby with greater force and rapidity and retains its impetus right up to the terminations of the umbilical arteries and the final portions of the umbilical mass As Rouhault showed in 1718 the circulation of the blood in the placenta depends primarily upon the foetal forces The idea of the union of the ventricular forces was first promulgated by Harvey

Finally Sabatier reproduced though at greater length a view met with at intervals in earlier publications namely, that the umbilical arteries of the foetus should not be described as originating from the internal iliac or hypogastric arteries as they appear to be if examined some time after birth While the foetus is in utero they arise from the aorta itself and on their course to the umbilicus they give off the external iliac arteries and the branches that later are to leave the internal iliac or hypogastric arteries These last are very small branches during foetal life of large stems i e in utero the umbilical arteries are the trunks of the branches from which later they will appear to arise The small size of the external iliac arteries and of the hypogastric branches is not surprising for the umbilical arteries are the ones that play the major role in foetal life and must receive the greater part of the blood of the descending aorta In consequence the lower extremities of the foetus, deprived of any excess of nourishment are feeble and thin by comparison with the superior extremities and the head, to which blood is supplied in much greater amount

There are many comments that one could make on Sabatier's hypothesis but one will suffice here namely that the Eustachian valve is absent from many animals even if it is present in the human foetus The absence from lower animals had been reported as noted above by Lancisi, it had also been mentioned later by Morgagni But comparative studies during the eighteenth century were largely wanting and the main object of research was the *human* foetus

Sabatier, however, as a result of much research, confirmed Winslow's view that the valve is normally greater in size in the foetus than in the adult He added that the decrease in size with age is often accompanied by *reticulation* (? cause) towards the free border of the valve

The main function of the valve, Sabatier thought, must be during intra uterine life, as Winslow had [in his first memoir] concluded What that function was, however, Sabatier had only succeeded in deducing after examining many times in the foetus itself, by means of a special technique, the situation, form, and direction of the valve "I saw," he wrote, "that it must prevent the entry into the right atrium of the inferior caval blood, and *direct it in its entirety towards the foramen ovale*, whence it passes into the left atrium and left ventricle, and from there into the aorta and the vessels going to the head and upper extremities"

The situation of the foramen ovale, he added, is greatly in support of this view, for it is placed not between the right and left atria, as commonly stated, but between the union of the venae cavae and the left atrium The right atrium is placed too far forward (i e sternally) to correspond exactly with the left atrium, but the two venae cavae, which lie behind (i e dorsally) and to the right, back on to the left atrium by means of their left and posterior (i e dorsal) portions It is, therefore, impossible for blood to pass from the right atrium to the left one Blood coming from the superior vena cava is guided into the right atrium, both by the direction of the vein, which descends very obliquely from right to left and from behind forwards (i e dorso-*sternally), and also by the Eustachian valve, which separates the two caval* streams Thus, it is only the inferior caval blood that can enter the left atrium through the foramen ovale

The foramen itself is below, rather than at the junction of, the two venae cavae This, and the anatomical structure of the parts, including the Eustachian valve, prevent any mixing of the two caval blood streams That coming from below, in large measure from the umbilical vein, goes into the left atrium That coming from above goes into the right atrium, and thence *into the right ventricle and pulmonary trunk*

From the Eustachian valve and foramen ovale Sabatier passed on to consider the ductus arteriosus Anatomical descriptions varied Some said it arose from the left pulmonary artery, some from the bifurcation of the pulmonary trunk Statements about its size were also conflicting He himself declared that it arose neither from the left branch nor from the bifurcation of the pulmonary trunk, but was itself the continuation of that trunk to the descending aorta The pulmonary arteries, he said, are small, in conformity *with the size of the undeveloped* lungs The right artery leaves practically horizontally, the left, which leaves soon after, goes almost perpendicularly upwards The calibre of the right is twice that of the left These directions and relative sizes persist after birth and throughout life

The function previously ascribed to the ductus had been that of diverting to the descending aorta the blood which would otherwise have had to pass through the lungs This, in Sabatier's opinion, needed amplification as follows The channel in question transmits to the descending aorta the

evidence, though the chemists might in the future find differences in the intimate composition of the blood in different vessels But, as first observed by Sabatier, the general blood mass of the foetus is in a way divided into two as a result of the dispositions of the foramen ovale and ductus arteriosus Bichat then went on to give Sabatier s schema without, strangely enough, mentioning the Eustachian valve In the foetus especially in the early stages there are two blood systems The first originates in the capillaries of the abdomen, lower limbs and placenta, and the blood derived from these sources passes up through the inferior vena cava into the left atrium and is thereafter ejected by the left ventricle into the ascending aorta and distributed to the capillaries of the head and upper parts The second system originates in these same capillaries, passes down through the superior vena cava into the right atrium and is ejected by the right ventricle into the descending aorta and distributed to the capillaries of the abdomen, lower limbs and placenta In other words the blood circulates in a figure of 8 in the first months from conception

Thereafter there is a slow change Through the gradual shutting down of the ductus arteriosus more and more blood passes through the lungs But throughout the greater part of foetal life, the left ventricle sends blood to the upper parts and the right ventricle to the lower ones The left ventricle is nearer the parts it supplies and its walls are thicker than those of the right ventricle hence the difference in development of the upper and lower parts of the body The closure of the foramen ovale goes pari passu with that of the ductus arteriosus Hence the inferior caval blood can no longer pass in its entirety to the left atrium, and an ever increasing part of it must go with the superior caval blood through the right side of the heart and the pulmonary circuit In consequence the ascending aorta begins to receive more blood than can be distributed by it through the carotid and subclavian arteries and the excess goes on down into the descending aorta for distribution to the lower parts of the body

The gradual retraction of the ductus arteriosus and foramen ovale can be seen if one examines foetuses at different stages In general there is a definite relation between the amount of blood sent by the right ventricle through the pulmonary circuit, and the amount sent by the left ventricle to the lower parts of the body As full term approaches, there is an increase in

(1) the amount of inferior caval blood that joins the superior caval blood and passes into the right atrium,

(2) the amount of right ventricular blood that makes the pulmonary circuit and passes into the left atrium and

(3) the amount of left ventricular blood that passes into the descending aorta

Bichat next went on to consider the foetal liver He first noted that there was a spur at the beginning of the ductus venosus, and that this spur was such as to oppose the entry of portal vein blood, but not of umbilical vein blood into the ductus He concluded from this that the ductus was intended to receive the residue of the latter blood The liver, he continued, is very copiously supplied with blood during foetal life Hence the relatively large

More important scientifically than Sabatier's memoir, but destined to receive little recognition in the immediate future,[1] was a communication that C F Wolff, the embryologist, made to the Imperial Academy of Sciences of St Petersburg in 1776 It was entitled "De foramine ovali, eiusque usu, in dirigendo motu sanguinis Observationes novae," and was illustrated by two copperplates Haller, as already mentioned, was the first or one of the first to grasp the importance of embryological research in connection with the problems of the foetal circulation Wolff, though in opposition to Haller on certain major counts (Needham, 1934, 197–), had the same outlook towards the subject and, through Meckel, he had to some extent derived from Haller

Two reasons that probably contributed very considerably to the relative failure of Wolff's memoir were, first, that it was confusedly written and, secondly, that the illustrations were complicated and probably incapable of conveying much to those who had little acquaintance with foetal dissections

He began by saying that in the past there had been disputes about the foetal circulation but not about the anatomy of the parts The foramen ovale was universally held to be single and unlike any other opening or duct in the animal body It was, however, less the unnatural idea of a single foramen between two vessels than the inexactness of current descriptions that had determined Wolff to investigate for himself As a result of his anatomical studies, he concluded that the human foetal atria were not in direct communication with one another, but that the inferior vena cava was interposed between them, and had independent openings into each of them The isthmus of Vieussens was common to both right and left openings, which were completed by the Eustachian valve and the valve of the foramen ovale respectively The isthmus was nearer the right than the left side and Wolff estimated that, towards full term, about two-thirds of the inferior caval blood would take the left-hand route, and about one-third the right-hand one He also examined the heart of the foetal calf In this there was no Eustachian valve, and there were certain other differences from the human But here again the isthmus of Vieussens divided the inferior vena cava, which terminated in short right and left branches The bifurcation was even visible on the external surface of the preparation

With respect to the ductus arteriosus, as opposed to the foramen ovale, Wolff's account was relatively poor, and he made no mention at all of the ductus venosus With respect to the foetal circulation, he believed that the amounts of inferior caval blood going to the left and right atria respectively varied according to the age of the foetus, but that all the superior caval blood went to the right atrium

Despite the rightness of his new outlook upon what has recently been styled the inferior/posterior caval channel and its terminal divisions, Wolff's work met with more opposition than praise, and the only definite supporters of it known to Kilian (1826) were Okel, Meckel, and Louron

After Wolff, Bichat published, in 1801, an account of the foetal circulation He divided the adult blood vessels into those with red blood and those with dark blood In the foetus no such distinction was possible on macroscopic

[1] The Radcliffe Library Oxford copy of Wolff's memoir was uncut before 1940 !

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size of the organ and its diminution on section. According to Portal, it is relatively largest up to the seventh month; the same authority noted that the umbilical vein blood went largely to the left side of the organ. This blood, while in the umbilical vein, was redder than that in the portal vein, according to statements made by Baudelocque to Bichat, and according to the latter's own observations on guinea-pig foetuses. The redness is, apparently, lost in the liver. After birth, there is a fall in liver volume with the cessation of the umbilical venous inflow, and the ductus venosus closes through the contractility of the tissue.

There must, Bichat stated, be some precise relation between the closures of the ductus venosus, foramen ovale, and ductus arteriosus, and between the increased activity of the lungs and decreased activity of the liver at birth. "Nous jugeons," he added, "de ce rapport sans le connoitre, parce qu'un voile est encore repandu, comme je l'ai dit, sur la circulation du fœtus."

In 1826 Kilian published not only a very much longer, but also a more thorough and comprehensive, account of the subject than had ever before appeared. It included a review of past work from Galen's time onwards, together with Kilian's own considerable contribution. He had studied the human circulatory organs from the third month of intra-uterine life onwards, and had gone far beyond his predecessors, Haller and Wolff, in this line. His material also was plentiful, so he was able to check each finding in a number of subjects. He dealt in turn with the inferior caval entry into the heart, the Eustachian valve, the valve of the foramen ovale and the foramen itself, the ductus arteriosus Botalli, the pulmonary arteries, the umbilical vein and ductus venosus Arantii, the umbilical arteries, and—to supplement the human data—with the heart of the unborn calf. Part of one of his Plates is reproduced here as fig. 9.

Kilian's historical survey was in some respects less accurate than the present one, but it was a great improvement on previous accounts.

With regard to the inferior caval entry into the heart, one may say that he followed Wolff but went farther, both in the details that he gave and also in the lucidity of their presentation.[1] The force of the inferior caval stream is responsible for the formation of the Eustachian valve and the valve of the foramen ovale, which are merely duplications or continuations of the membrana intima of the vein. The valve of the foramen ovale is not necessary in order to prevent reflux from the left to the right atrium. For in atrial diastole there is no question of blood so passing, and in atrial systole it goes naturally from the full atria into the empty ventricles. On the other hand, Winslow and others were wrong in thinking that the sole function of the valve was the post-natal closure of the foramen, for it reaches its maximum development by the thirtieth week of pregnancy. The inferior vena cava is wider at its entry into the heart than at its passage through the diaphragm. It opens into both left and right atria, the two openings being halves of one and the same channel. The foramen ovale is thus nothing but the opening through which the left stream of inferior caval blood enters the corresponding

[1] The précis of Kilian's work which follows here contains no comments by the present writers except for the footnote mentioning Ziegenspeck's criticism. The rest is pure Kilian.

atrium The function of the valve of the foramen ovale is to prepare for, and to effect, the gradual closing off of the inferior vena cava from the left atrium and to promote its complete transfer to the right atrium The Eustachian valve is supposed to guide blood from the inferior vena cava to the foramen ovale, but the direction of the vein itself is adequate to ensure this Further if the valve does so direct the ascending blood to the foramen, then the whole of this blood must go to the left atrium as Sabatier postulated and not merely the greater part of it, as Haller stated For, once the left atrium is full it contracts and as systole is simultaneous in both atria no blood can pass to the right atrium after the left has been filled But according to Kilian's findings, part of the inferior caval blood does reach the right atrium so the Eustachian valve cannot have the above mentioned function What it actually does is to form the opening of the inferior vena cava into the right atrium, and to guide the inferior and superior blood streams entering that atrium so that they do not obstruct each other Injection experiments show that the main effect is upon the superior caval flow rather than, as usually stated, upon the inferior one

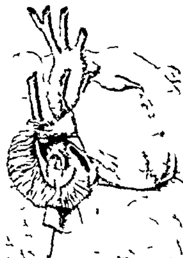


Fig 9.—From Kilian (1826) The main part of Plate I showing the heart and great vessels of a human foetus at the beginning of the fourth month The right atrium has been opened up and the heart as a whole somewhat displaced in order to display certain structures The probe passes up through the inferior vena cava then lies between the expanded Eustachian valve and the valve of the foramen ovale and finally disappears from view to the left of the arched isthmus of Vieussens within the cavity of the left atrium The superior caval opening into the right atrium and the right atrio-ventricular orifice are clearly seen

From the above survey of the inferior caval entry Kilian passed on to consider more particularly the Eustachian valve and the valve of the foramen ovale stating in passing that neither was a valve in the proper sense of that word The Eustachian valve is in full development at the end of the third, and in the fourth month of pregnancy (fig 9) after which it becomes relatively smaller and undergoes changes from its original position and lie It shows no fenestration, as several anatomists have believed, when fully developed

The valve of the foramen ovale is present between the second and fourth month of pregnancy (fig 9) but undergoes many changes in position and lie before reaching its full development in the seventh month The prolongation of the tunica intima of the inferior vena cava into the left atrium is very much greater than into the right in correspondence with the much stronger blood flow from the vein into the left atrium In the last months of pregnancy muscle fibres are visible in the valve of the foramen ovale, the texture of which is much firmer and stronger than that of the Eustachian valve

No one except Wolff and his supporters has had a correct view about the foramen ovale All other writers regard it as a simple opening in the interatrial septum that can be closed on the left side by its valve The literature on the subject is very great and even the exact connotation of the term

"foramen ovale" is not universally the same The foramen is not a perforation of the interatrial septum, but is posterior to that septum The direction and lie of the isthmus of Vieussens and of the foramen are not easy to describe because of the very considerable rotation of the foramen from its first appearance up to birth and even after birth

The ductus arteriosus is generally said to be an important branch, or a continuation, of the pulmonary artery [i e pulmonary trunk] and, apart from Roderer and Bichat, who had no real basis for their statements, few writers have properly assessed its function Actually the pulmonary artery, together with the ductus, is the *abdominal aorta* so long as the ductus remains open, i e during the whole of foetal life In exactly similar fashion the artery rising from the left ventricle is the *cerebral aorta* The blood for each aorta comes solely from the ventricle with which it is connected

The basis for the new view is provided by

(1) the *developmental story of the cardiac vascular trunks*,
(2) the anatomical lie and disposition of the vessels in question,
(3) the very obvious evidence drawn from the doctrine of the circulation,
(4) injections with wax masses of different colours, and
(5) the findings of pathological anatomy [1]

As a result of his various evidence, Kilian proposed to discontinue in the rest of his account the use of the terms *ductus arteriosus, pulmonary artery*, and *ascending* and *descending aortae*, and to substitute for them the terms *cerebral* and *abdominal*, or *left* and *right*, *aortae*

He passed next to a consideration of the blood flow through the lungs of the foetus There is, he said, a generally accepted belief—though it is entirely unsupported by any direct evidence—either that this pulmonary flow is non-existent or else that it is relatively small Actually, the blood supply to the foetal lungs is as copious as, and perhaps relatively greater than, that to the adult lungs From the fourth month of pregnancy to full term the development of the pulmonary vessels keeps pace with that of the lungs themselves, so that it is ridiculous to speak of a *slight* pulmonary circulation There is also a copious bronchial arterial supply

To previous accounts of the umbilical vein Kilian added little He held, in opposition to Bertin and others, that the ductus venosus is not a continuation of the umbilical vein, but of the main trunk of the portal vein It corresponds, in the circulatory system of the liver, to the ductus arteriosus in that of the lungs With regard to the umbilical arteries, Kilian stated that in the third to fifth months of foetal life they arise direct from the descending aorta, and are only later taken into the compass of the hypogastric arteries

From the cardiovascular system of the human foetus Kilian passed on to consider the inferior vena cava in the heart of the foetal calf The heart of the four to six weeks' calf differs from the human in five respects

(1) its deeper descent and relatively larger size,

[1] Among the cases quoted by Kilian was one described by Steidele in which the lumen of the aorta was completely obliterated at the point where in the foetus it commonly—according to Kilian—shows a narrowing i e between the origin of the left subclavian artery and the union of the ductus arteriosus and aorta This part of the aorta is Nicholls channel of communication Ziegenspeck (1905) criticized Kilian for basing too much on a single pathological instance

(2) the absence of a foramen ovale providing direct communication between the two atria,

(3) and (4) the absence of the Eustachian and Thebesian valves and

(5) the completely different structure of the valve of the foramen ovale

The atria communicate only indirectly through the right and left branches of the inferior vena cava and the inferior vena cava itself This truth, of fundamental importance for the doctrine of the foetal circulation, is even more evident in the foetal lamb, which retains the double branching of the inferior vena cava and the prolongation of the left branch into the left atrium right up to birth The study of the foetal calf's heart thus confirms the impressions obtained from the study of the human foetal heart with regard to the double opening of the inferior vena cava the import of the foramen ovale, and the misnaming of the valvulae Eustachii and foraminis ovalis

In the final section of his article Kilian propounded his views of the circulation in the foetus It would he said, be a thankless task to work out schemata for all stages but one ought to find a theory applicable to the period during which the heart undergoes no further fundamental changes This period may be said to begin when the interventricular septum is complete both atria are developed, and the valves of Eustachius and of the foramen ovale are in full activity The fourth month of foetal life satisfies all these requirements for from then until the eighth month there are no more fundamental changes in the heart

After criticizing what he called the theories of Galen and Harvey and of Sabatier Bichat and Richerand respectively, Kilian went on to state his own The blood from the placenta, he wrote passes via the umbilical vein to the liver where it divides into two unequal portions Much the larger one makes its way through the liver while the other, much smaller, one passes direct to the inferior vena cava through the ductus venosus In the short but wide channel of the thoracic portion of the inferior vena cava the placental blood mixes with that coming from the lower extremities, pelvic viscera and so forth

The strong stream of blood reaches the heart where it divides into two parts One of these passes unmixed into the left atrium while the other contributes to the filling of the right atrium The left atrium therefore, contains a mixture of part of the inferior caval blood with that from the pulmonary veins The right atrium, on the other hand contains a mixture of the rest of the inferior caval blood with that from the superior vena cava

So soon as the atria are full, which is a simultaneous occurrence in both, they contract and their contained blood passes into the corresponding ventricles These then contract in their turn and the twin arterial circulation begins The blood from the left ventricle passes into the ascending aorta and its three ascending branches only not a trace of it reaches the descending aorta The right ventricle on the other hand directs its blood via the large vascular bed of the pulmonary artery and ductus arteriosus, into the descending aorta only not a trace of it reaches the ascending aorta Thus, from the time both atria are full, blood cannot mix in any part of the circuit, for the two arterial systems are completely separate

The blood going by the ascending aorta returns through the superior vena

cava, that going by the descending aorta makes the placental circuit The most difficult task that remains is the elucidation of the circulatory conditions in the placenta itself, and of the connection between the placenta and the walls of the uterus

From what has been said above, it is obvious that the most important differences between the foetal and adult circulatory organs is that in the foetus the inferior vena cava helps to fill two atria, and that there is a double aorta

The left branch of the inferior vena cava has for the foetus exactly the same physiological significance that the pulmonary veins have after birth, for through it the most enlivening [i e arterial] blood passes to the left heart In the early stages of intra-uterine life the inferior vena cava supplies a greater proportion of the blood going to the left heart, for the pulmonary venous return is small Later, with the increase in this return, more inferior caval blood is diverted to the right heart and this diversion raises the quality of the blood returning by the pulmonary veins, so that the quality of the mixture in the left heart is not seriously impaired The left branch of the inferior vena cava has, thus, the important function of preparing the left heart, both dynamically and mechanically, for its future vocation

The increase in inferior caval flow to the right side of the heart in the later stages of pregnancy means a rise in the quality of the blood coming to this side In addition, as the superior caval flow still comes to the right atrium, and the inferior caval contribution is relatively increased, the right heart tends to increase in size as compared with the left

In the placenta the foetal blood undergoes a change analogous to that which the post-natal blood undergoes in the lungs Hence the left branch *of the inferior vena cava supplies the left ventricle of the foetus with blood* that is not dissimilar to that supplied to this same ventricle by the pulmonary *veins in post-natal life*

In the foetus there is a greater circuit for the blood to traverse, for it has to pass to structures outside the body In consequence, it is necessary to employ more power to drive the blood around, and this is ensured, not by adding to the work of the left ventricle, but by both ventricles dealing with the propulsion of blood into the aorta, which is so divided that the force to be expended by each ventricle is approximately the same Research has shown that the strength of the walls of a ventricle varies directly as the extent and intensity of the circulation effected by it The right ventricle has in the foetus, where it sends blood to the placenta, a task analogous to that which it has after birth, when it sends blood to the lungs, for, as we have seen above the placental function is analogous to the post-natal pulmonary function As more and more blood comes from the inferior vena cava to the right heart during the later stages of pregnancy, so more blood ejected by the right ventricle passes into the first branches of the "abdominal aorta," i e into the pulmonary vessels

It is obvious, from all that has been said, that the peculiar structure of the inferior vena cava, where it enters the atria, and the changes undergone by it, are the prime causes for the heart and great vessels developing as they do

In the foetus the left ventricle performs duties not too dissimilar to those

that it is to perform throughout life i e the propulsion into arteries of blood that has been (more or less) revivified The right ventricle, on the other hand must not only send blood to the placenta and thereafter to the liver for such revivification but it must also supply the lower part of the body with blood suitable for its nutrition If the inferior caval inflow into the right heart were not increased, as we have seen it to be, in the later stages of pregnancy, the blood in this right side would be even less pure than it is, in comparison with that in the left ventricle In consequence, there would be a poorer development of the lower half of the body as compared with the upper

In contrast to the physiologists who said that all the special foetal cardiac mechanisms are there for the purpose of by passing the pulmonary circuit Kilian believed that the manifold changes undergone by the cardiovascular system, including the increasing flow through the pulmonary circuit as pregnancy progresses are preparations for the complete independence of the two sides of the heart that is to occur with the first respiratory activity

Intra uterine life as exemplified by the vascular system, is a preparation for the highest form of life This system must however (and in this it is at a disadvantage as compared with some other organs), be so advanced by the end of pregnancy that it can change over at once to its post-natal state with the onset of respiration

With this respiratory activity there is a great increase in the blood flow from the ' abdominal aorta into the pulmonary vessels and a corresponding decrease in that from the same vessel into the umbilical arteries When the pulsation in these arteries drops, one knows that the pulmonary circuit is functioning well and that one can sever the umbilical cord When the placenta is away there is an increased venous return to the right heart and thereby an increased flow into the pulmonary vessels The return to the left atrium is greatly increased and the so called valve of the foramen ovale, which up to birth had been lying ever closer to the interatrial septum is now pushed right up against that septum so that the opening of the left branch of the inferior vena cava into the left atrium, i e the so called ' foramen ovale is no more With the increased flow into the lungs from the " abdominal aorta the left ventricle *has to take* over the supply of those parts that were not its concern in foetal life This can only occur through a dilatation of the narrow point that has been described as occurring between the cerebral and abdominal aortae in the foetus, and the consequent development of the single post natal aorta to which one is accustomed

Eight years after Kilian s *article appeared* i e in 1834 one of his pupils, Knabbe produced a remarkable doctorate thesis entitled *Disquisitiones historico criticae de circulatione sanguinis in foetu maturo no is observationibus anatomicis exaratae* The bulk of the book is, as the title indicates historical and critical and it is of use to the modern historian provided he verifies the statements made by the author Apart from this elaborate introduction the work obviously derives from and supports, Kilian In the latter part of the nineteenth century Preyer lent his copy to Ziegenspeck and the latter translated it into German page by page for his own use This explains why Ziegenspeck and those who derived from him, appreciated at its right worth

Wolff's contribution but in certain important respects misrepresented that of Harvey

In 1835 Reid published the results of injection experiments carried out upon three dead human foetuses In a note printed later in the same year, he wrote that the injections "go to confirm the opinion which Sabatier, from a careful examination of the *structure of the parts, entertained* of the use of the Eustachian valve The observations of Sabatier, although approved of and illustrated by Bichat, seem scarcely to have satisfied the generality of anatomists and physiologists, that it could possibly prevent the intermixture of the two currents, in the manner he described, so that we frequently find this opinion referred to, as the supposed use of the valve, and in two of the latest works on physiology, those of Magendie and Dr Bostock, the use here assigned to it is by *the former strongly stated to be impossible*, and by the latter it is treated as a fanciful hypothesis The careful examination of the *foetal heart in situ* must tend powerfully to remove the scepticism which usually exists on this subject"

He then gave an account, rather similar to that of Sabatier, of the positions of the foramen ovale and the Eustachian valve, finishing up with the remark that "the course which the currents take in passing along the aorta and *pulmonary artery is confirmatory of injections of these arteries in the foetus*, made by Kilian"

The above note about Reid's work is inserted here not because of any particular merit of his injection experiments, which are open to a number of criticisms, but because his comments give some idea of current opinion in at least one country So far as that country—Great Britain—was concerned, Reid's experiments would appear to have helped in reviving Sabatier's schema For in Herbert Mayo's *Outlines of human physiology*, published in 1837, the routes followed by the foetal blood were presented as they had been outlined by Sabatier and, in the part dealing with the inferior caval flow, though Reid was not mentioned by name any more than Sabatier had been, it was stated that "injections on the dead subject verify the correctness of this hypothesis" On the other hand, the route suggested for the superior caval flow, i e into the right atrium and ventricle, was "fairly presumed" to hold in the living foetus, "because in anatomically preparing the foetal heart and injecting it, it is found that wax thrown into the upper cava pursues this course" Incidentally, Mayo mentioned the coronary venous return as flowing with the superior caval blood into the right atrium and ventricle, but did not refer to the coronary arterial flow, though this should be of importance in Sabatier's schema But, except in very recent reviews, writers on the foetal circulation have shown a surprising forgetfulness of the coronary circuit, and perhaps Mayo should be praised for mentioning the coronary veins rather than blamed for failing to mention the arteries!

A similar, though shorter, description of the foetal circulation was presented, in 1856, in Todd and Bowman's *The physiological anatomy and physiology of man*, and without examining every textbook one may presume that Sabatier's concept was by then widely accepted in Great Britain

In the tenth edition of Quain's *Anatomy*, forty years later, the account was

certainly qualified by such phrases as "it is believed" and the possibility was mentioned that a small part of the inferior caval stream might mingle with that of the superior vena cava, and pass into the right heart But in general the schema of the foetal blood flow presented in this 1896 Quain was that which Sabatier had put forward in 1774, and both he and Reid were mentioned by name though without references In addition there was the following note "A striking confirmation of the extent to which the last mentioned division of the two currents of the foetal blood may take place, without disturbance of the circulation up to the time of birth is afforded by the examples of malformation in which a complete obliteration has existed in the aortic trunk immediately before the place of union of the ductus arteriosus with the posterior part of the aortic arch'

Writing in America in 1909, Pohlman referred to Sabatier's concept as the theory then prevalent

In France according to Reid, it was opposed by Magendie after being warmly supported by Bichat Later, it would appear to have been generally accepted just as it was in Great Britain Such at all events is the impression that one gets when one reads Marey and Carlet's very clear account (1875) in *Dictionnaire encyclopedique des sciences medicales* In this account incidentally, the writers spoke of the placenta as being an organ of nutrition as well as of respiration Both uses must have been mentioned with some pride by Frenchmen in as much as Lavoisier's work had introduced the modern phase of respiratory study and Claude Bernard in 1858 (Needham 1934, 86) had discovered that the glycogenic function of the liver is undertaken for the foetus by the placenta, thus justifying Aranzi's intuition of three centuries earlier Marey and Carlet considered that *practically all* the inferior caval blood from the umbilical and portal veins and from those of the lower extremities passed into the left atrium, being guided thither by the Eustachian valve On the other hand, in their view, the tubercle of Lower turned the superior caval stream away from the inferior caval stream so that the former passed *practically completely* into the right atrium and ventricle

In Germany also at least up to about 1880 Wolff's main finding remained not only unrecognized but also unknown In the textbooks of anatomy physiology embryology and midwifery one found reproduced now the old Harveian doctrine now that of Sabatier, and now a mixture of the two (Ziegenspeck 1884) One has only to read the main part of Preyer's *Specielle Physiologie des Embryo* 1885 to realize how confused were current ideas Yet the same book included an article by Ziegenspeck (Ziegenspeck, 1884) in which he confirmed Wolff's finding and in which he also gave directions for making a demonstration model of the terminal bifurcation of the foetal inferior vena cava He had two years previously produced an inaugural thesis on similar lines [1] and it is certainly strange that his work had not been properly appreciated by Preyer Ziegenspeck had confirmed Wolff's view, first in a series of guinea pig foetuses and then in a smaller number of human and ovine foetuses He realized at the same time that minor details in

[1] The present writers have not had access to a copy of this thesis but the 1884 publication gives such details as are necessary

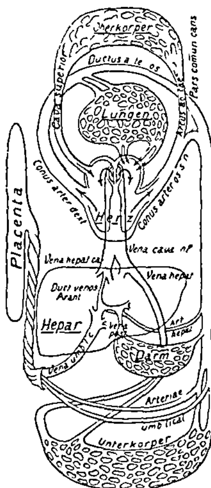


FIG 10.—From Ziegenspeck (1905) fig 9. The correct schema of the foetal circulation according to the author. For details see the original paper.

Wolff's account, e.g. his ideas of the origin of the terminal branches of the inferior vena cava, had probably to be modified in the light of recent embryological findings. He referred to this at greater length in a later publication (Ziegenspeck, 1905), in which he gave detailed measurements of various parts of the human foetal cardiovascular system, and in which he reproduced some very convincing figures of the bifurcation.

There is no need to summarize here all that Ziegenspeck wrote, for most of his published work is reasonably accessible. One must, however, attempt to explain why, despite all his efforts, the correct outlook upon certain features of the foetal cardiovascular system failed to become generally adopted. For fail, so far as one can make out, it did. Two factors in particular, one imagines, may have been concerned. The first is that there was no experimental proof of the correctness of the deductions made from studies of the structure of the parts. The second is that, in 1905, he superimposed on his anatomical findings a new, and—one imagines—unacceptable, schema of the foetal circulation (fig. 10). It was a very arithmetical concept of the blood flow in the foetus and, in the present writers' opinion, it was invalidated from the beginning by the complete omission from consideration of certain, not unimportant, inflows. For, with the inclusion of these, the arithmetic would have been at fault. Despite this, Ziegenspeck's general contribution to the subject was a very substantial and timely one, and he deserves much credit for it.

And there one must bring to an end the third part of this historical survey. A complete account would have included much more, for from Kilian's time onwards there was a great increase of knowledge about the embryology, histology, comparative anatomy, and so forth of the constituent parts of the foetal cardiovascular system. But much of this is well known to readers, and some at least of the literature will be referred to in later sections of this book. So the omissions are less important than they would have been in respect of the seventeenth and eighteenth centuries, the literature of which is less generally known and less readily accessible.

(iv) THE PERIOD OF EXPERIMENTAL RESEARCH

This period was initiated by Pohlman, who in 1907 reviewed the more important theories of the blood flow through the foetal heart, and gave a preliminary report on his own experimental findings. A longer account,

together with a more detailed historical survey, appeared in 1909, and fifteen years later still Pohlman published another paper

In his second account of his experimental work, he wrote as follows (1909, 91–2) 'It became evident from the varying results obtained through observation and injection of the dead fetus, that if any further work was to be done on the course of the blood through the fetal heart, it must be undertaken in the living animal and with the placental circulation intact The fetal pig was chosen because of the accessibility and abundance of material and the several propositions demanding an answer through the experimental method were considered as follows

I Is the ventricular capacity an equal one in the fetal heart ?
'II Is the pressure exerted by each ventricle equal
III What is the course of the blood entering the heart through the cava inferior
'IV What is the course of the blood entering the heart *through the cava* superior '

Pohlman obtained the foetuses by removing them, plus the containing uteri, from sows killed in the abattoir He noted that foetuses can live for many *hours* after the death of the mother, whereas his experiments were usually *concluded* within half an hour, and sometimes within a quarter of an hour, of such *death*

To answer his first question Pohlman occluded suddenly *in two foetuses*, at the end of atrial systole, the ventricles and aortae He *then measured* the contents of the ventricles and found that of the right one equal to that of the left

To answer his second question he introduced equal sized capillary tubes into the two *ventricles of the* foetus He saw the blood mount evenly in the two tubes

To answer the third and fourth questions, he made intravenous injections of corn starch granules *suspended* in saline and thereafter carried out micro-counts of the granules in samples of blood taken simultaneously from the right and left ventricles

He *concluded* as follows (1909, 98) 'The results from our experiments in the living embryo lead to the following statement that the ventricular capacity and pressure is an equal one that the foramen ovale does afford communication between the two auricles, that the blood of the two cavae mixes in the right auricle and that mixed blood passes through *the foramen* ovale We agree, *therefore* with the theory of Galen Harvey and believe to have established *it* through experimental evidence A few pages later he added this note We *trust* that this article carries *conviction* with it and that the coloring *of* diagrams to render the impossible theory of Sabatier clear to the student will hereafter be omitted The arrows to indicate the course of the blood through the fetal heart may be replaced by *the statement*—the blood of the two caval veins mixes in the right auricle and mixed blood passes through the foramen ovale into *the left* auricle to make up for the deficient pulmonary return (the theory of Galen-Harvey) '

It seems almost unfair to criticize the man who first realized that the foetal circulatory problems must be solved by experimental methods, but one must add to the objections that he himself raised (1909, 95) the facts (1) that the uteri he used had had no circulation for some time previous to the experiments, and (2) that the operative interference with the thorax and its contained viscera was considerable. In addition, one must point out that Galen had no theory of the foetal *circulation*, and that Harvey did not include in his account any statement about the mixing of the two caval streams within the right atrium, with subsequent passage of part of the mixture through the foramen ovale into the left atrium.

In his third paper, in 1924, Pohlman dealt with the comparative embryology of the foramen ovale, ductus arteriosus and ductus venosus, matters with which one is not directly concerned in this section of the history.

In 1928 Kellogg published the first of his two papers. He had made about two hundred observations on pig foetuses, removed with the uteri as in Pohlman's experiments. Into the umbilical or external jugular veins of about one hundred and twenty-five of the foetuses he had injected suspensions of corn-starch, or of Indian ink, in normal saline. Thereafter he had seen the apices of both ventricles blanching, or blackening, simultaneously. "These observations," he said, "while not primarily of a quantitative value, constitute definite evidence proving beyond a doubt that the two caval streams do mingle in the right atrium, whereupon both ventricles receive mixed arterio-venous blood." To supplement the direct observations, he injected corn-starch suspensions as Pohlman had done, and thereafter made comparative granule counts in blood samples from the ventricles. He also made injections into the umbilical veins of five puppies delivered under ether anaesthesia, with the maternal and foetal circulations continuing. While the results showed greater variation than those of the pig series, "they nevertheless afford very important evidence in support of the Harvey-Pohlman theory, since they are the first obtained on animals in which both the maternal and fetal sides of the placental circulation were intact and other general conditions approached normality."

In his second paper (1930) Kellogg, criticizing the Sabatier hypothesis, said that "two relatively slow moving blood streams were supposed to cross within the right atrium without mixing." He then noted that, while Pohlman's work was the first done with living foetuses, "it has not met with much acceptance. Perhaps this is due to the fact that the number of animals used was small." His own more extended experiments, reported in 1928, had been followed by further ones, carried out mainly upon foetal puppies. These were delivered one at a time by Caesarean section, and respiration was prevented by retention of the membrane surrounding the head and neck. Blood samples were taken from both ventricles, from the umbilical vein, and from the superior and inferior venae cavae of the foetus, and from the uterine artery and vein of the mother. Thereafter blood gas analyses were made by Van Slyke's micro-method, and from a study of the results Kellogg came to certain conclusions that were later inserted in textbooks of physiology and so forth. There were, however, several criticisms that could have been made

at the time, and even stronger ones have since become possible as the techniques employed in foetal studies have been improved and potential pitfalls noted It is doubtful if anyone would to day support, to any serious extent, Kellogg s contentions and there is, therefore, no need to repeat criticisms that have already proved effective, or to add certain others that have not yet appeared in print Kellogg s real contributions were (1) that he initiated experiments in which the foetus was delivered by Caesarean section, the foetal and maternal circulations were retained and foetal respiration was prevented, and (2) that he realized the possibilities of blood gas analysis as a technique for the solution of certain foetal problems

To Barcroft and his School at Cambridge is due the main credit for the improvements that followed both on the operative side and also on that of blood gas analyses One need not speak at length about these, for the work is well known to readers and a full account is, presumably, appearing in Barcroft s new book on the physiology of the foetus But the present writers who have co operated with him have been impressed with the precautions that he takes to ensure that both mother and foetus are in the best possible condition, and also with his dictum that it is satisfactory if one secures a single accurate determination of permanent value, from any particular foetus They themselves have, on more than one occasion attempted more, and perhaps more can reasonably be expected with such a technique as cineradiography, which involves less interference through operative procedures and the like But they would like to pay their meed of tribute to Barcroft for the outstanding contributions that he has made to foetal physiology, and this is perhaps a fitting place in which to do so

The best blood gas analyses, however, can give only indirect information about the foetal circulation, and hence Barcroft and Barron in 1938, united their experience of the foetus to Barclay, Franklin and Prichard s experience of cineradiography, and the combined Cambridge and Oxford team in determining times of functional closure for the ductus arteriosus, obtained, as already stated the first direct records of the circulation in the intact foetus

There one may conclude this somewhat incomplete, but perhaps adequately indicative historical survey As has been said, a fuller account of the advances from Harvey s time onwards may be offered at a future date for publication in *Annals of Science* the journal in which Part I of the longer survey has already appeared

PART TWO

CHAPTER II

The Actual Course of the Blood Flow, determined by Means of Cineradiography, in the Mature Foetal Lamb

THIS Chapter is concerned with one special aspect of our researches on the foetal circulation and cardiovascular system, namely, with the radiographic studies which we have made (initially in collaboration with Barcroft and Barron and subsequently, on occasion, with Barcroft alone) to determine the course of the blood flow in the intact foetus, delivered near term by means of Caesarean section A short account of our techniques has been included in order that readers may have some idea of the conditions under which the radiographic records were obtained The techniques in question were evolved step by step as the needs of the research became apparent, and they proved adequate for their immediate purpose, on the other hand, it would be idle to claim that, even in their latest form, they have reached perfection or finality

Our chief concern in the operative procedures was to cause the minimum of interference with the natural conditions of the foetus, so that the radiographic records obtained might present a picture of the circulation approximating as closely as possible to that which occurs in normal circumstances Both operative and radiographic techniques were far from simple, and a team of ten or twelve persons was required to co-operate, at times very rapidly and always without a single mistake, if the experiment was to be a success

(1) OPERATIVE PROCEDURES

For the technique of Caesarean section and certain procedures for dealing with the foetus we are indebted to Barcroft and Barron, whose experience in these matters is unsurpassed, to their collaboration with us in the early stages of our work we owe much

Some days before the operation, the ewe was radiographed in order that the number of foetuses might be known On the day of operation, the wool was clipped close to the skin over the abdomen and, if the anaesthetic was to be given intravenously, over one side of the neck The anaesthetics used were intravenous urethane, intradural borocaine, or subcutaneous procaine (syn, novocaine) for the ewe, and subcutaneous procaine for the foetus Two factors had to be considered in the administration of urethane and borocaine, namely, the adequate anaesthesia of the ewe, and the minimal depression of the foetus

When anaesthesia had been produced, the skin over the ewe s abdomen was incised in the mid-line between the sternum and the mammary glands (udder), and the cut was then carried to both sides close to the bases of these last The

subcutaneous veins crossing the lines of the incisions were divided between ligatures and after further injections of procaine, the skin was freed for a short distance on either side of the main line of incision Finally, the abdomen was incised along the linea alba, and a ligature was passed ready to close the upper part of the wound before the records were made The uterus (or, if there were two foetuses, one horn of it) was then delivered, and the lie of the foetus ascertained A small incision was made through the thin uterine wall in its least vascular part and near the head of the foetus, and a certain amount of amniotic fluid was collected and poured into a condom that would be used as a "nose-bag' If there were to be intravenous injections into a jugular vein of the foetus the cannula was often inserted under local anaesthesia after delivery of the neck, the head and the rest of the foetus remaining meanwhile in utero When all the recording arrangements had been checked, and the ewe correctly positioned in respect of the recording apparatus, the uterus was incised farther, the foetus delivered and its muzzle at once covered with the filled nose bag to prevent respiration If the first injection was to be a femoral or mesenteric one the cannula was now inserted under local anaesthesia The ewe was then rolled over on to its left side and, with the umbilical cord properly safeguarded and all undue traction on the cotyledons avoided, the foetus was placed in position (usually the left lateral one) for recording, the fore- and hind limbs were held in extension Finally, a syringe and pressure tubing[1] containing contrast medium at body temperature were connected with the cannula and recording was effected during the injection of the medium If the injection was to be into one of the umbilical veins within the cord no cannula was used the injection being made instead through a wide bore needle After the injection the needle was withdrawn and the part covered with gauze soaked in fresh mucilage of tragacanth Prior to such umbilical injections Barcroft commonly sprays formol saline over the part where the needle is to be inserted, but we found this procedure unnecessary and discarded it To ensure success the needle had to be inserted at the first attempt, for the vein is very sensitive to mechanical stimulation and will contract down if over stimulated The above account of the procedures makes somewhat long reading but in practice they were very rapidly carried out, and recording has sometimes begun in less than 30 seconds from delivery in cases in which the venous cannula was inserted in utero

Records obtained so soon after delivery, with the filled nose bag preventing respiratory reflexes and with the placental circulation continuing and adequately safeguarded were considered to give a picture not essentially different from that of the normal, intra uterine foetal circulation In order to get information about the changes occurring at and soon after birth, other records were made at intervals after the nose bag had been removed and the cord divided Here again there was operative interference with the normal procedure, but there is every probability that the experimental records so obtained provide a picture essentially similar to that which occurs under natural conditions Lambs normally bleated soon after the nose-bag had been removed, and they

[1] Pressure tubing was used not to withstand the pressure of injection for that was not unduly high but because such tubing contains little fluid and because it does not kink

have on occasion risen to their feet and even walked about in the intervals between the records

After the cord had been divided the ewe was killed with the ordinary humane killer of the abattoir When the experiment was concluded the foetus was killed by an overdose of a general anaesthetic, and was usually fixed in formol saline in order that the anatomical findings might later be compared with the radiographic records

(ii) CONTRAST MEDIA

For the post mortem study of the foetal cardiovascular system, intravascular injections of sodium iodide, dissolved in its own weight of water, provide excellent contrast On the other hand, such a solution is toxic to the living animal, hence, for our studies of the circulation in the intact foetus other radio-opaque media were employed These were of two general types

(a) Substances freely miscible with the blood, e g *thorotrast, uroselectan B, perabrodil*, and

(b) Oily substances that are not miscible with the blood, e g lipiodol

Thorotrast is a proprietary colloidal preparation containing 25 per cent thorium dioxide in association with a carbohydrate It mixes well with the blood, gives very good contrast and, even in high concentration (up to 10 c c per kg body weight), appears to be fully tolerated In certain animals, e g the cat and the dog, it is removed from the blood fairly rapidly and concentrated in the liver and spleen In the foetal lamb it is not so removed but remains in circulation (Barclay, Franklin, and Prichard, 1942, c), thus hampering the observation of subsequent injections So far, therefore, as this animal was concerned, it was found necessary to limit the use of thorotrast to experiments in which only a single injection was required

Uroselectan B is a proprietary preparation of iodoxyl which gives good contrast and is rapidly eliminated from the blood stream via the kidneys (Weatherall, 1942) Unfortunately it appeared to be toxic to foetal lambs in the dosage required for our studies and its use was abandoned in favour of that of perabrodil

Perabrodil is a proprietary preparation of diodone, diodrast, pyelosil, and pylumbrin are similar ones (Weatherall, 1942) Like uroselectan B perabrodil gives good contrast and is rapidly eliminated via the kidneys It was well tolerated by the foetal lamb, and in the 35 per cent solution it was the medium of choice for nearly all our more recent studies On account of its rapid clearance it is particularly useful in experiments designed to determine the time of functional closure of the ductus arteriosus and other foetal channels, for a series of injections can be made, at intervals of as little as five minutes, to provide information as to the state of the channel in question at various lengths of time from delivery

Lipiodol can be injected unchanged, but emulsification with normal saline (one part of saline to three or four of lipiodol) facilitates the injection, reduces the size of the droplets and thus allows them to circulate more freely It is an excellent substance from the radiographic point of view, for each droplet gives a conspicuous shadow as it is carried along in the blood stream Physiologi-

cally, however, lipiodol has definite demerits for the globules are often pushed out of the axial stream into the slower peripheral one with the result that they do not show the true rate of blood flow and appear to adhere to the walls of the vessels More important still, if they are of radiographically useful size, they cannot pass through the capillaries and hence they produce progressive stasis in the parts to which they are distributed In consequence, it is only during the first few seconds after injection that they give a picture of the blood flow that approximates to the normal In our experiments the use of lipiodol has been confined to injections recorded by indirect cineradiography The films thus obtained have been of value chiefly in confirming evidence afforded by other techniques which are less open to fallacy, but they have also provided useful supplementary material for a detailed study of the course of the blood flow for by a frame by frame analysis it is possible to plot the movement of individual droplets In addition, these films are of value for demonstration purposes for on projection the stream of moving droplets presents a more spectacular appearance than that provided by the less sharply defined, continuous stream of one of the miscible contrast media

All contrast media, syringes, and rubber and metal connections, were kept at body temperature until the injections were made The total amount of medium injected into a vessel was varied according to the requirements of the particular experiment, but the amount to be injected per second was planned to correspond with the estimated normal blood flow per second through that vessel so as to obviate any undue rise of venous pressure The veins into which injections were made were the jugular, femoral and mesenteric veins and one or other of the umbilical veins within the cord

(iii) RADIOGRAPHIC TECHNIQUES

In our studies of the foetal circulation we have used both the direct and the indirect methods of cineradiography A detailed description of the apparatus employed is beyond the scope of this book and has been published elsewhere (Barclay Franklin and Prichard 1940) but, in order that the reader may be able the better to evaluate the radiographic records reproduced later in this Chapter a brief account is given of the main principles of the two methods by which these records were obtained

The direct and indirect methods differ fundamentally in principle from one another In the *direct* method the image is recorded directly *on X-ray film* and thus a series of actual, life size radiographs is taken at a rapid speed In the *indirect* method a fluorescent screen takes the place of the X-ray film, and the image on this screen is photographed with a cinema camera

The X-ray apparatus employed in obtaining records by both the direct and the indirect methods consisted of a twin valve set and a 10 KW non shock-proof tube

The direct method —The direct " camera "[1] consists of a lead lined box, with an aluminium window (5 inches by 5 inches) in the upper surface through

[1] This apparatus was constructed by the Cambridge Instrument Co Ltd the greater part of the cost being met by a grant from the Medical Research Council

which the exposures are made (fig 11) The subject is placed directly on this window The camera is loaded with a spool of standard double-coated X-ray film 5 inches wide, and when it is set in motion the film is drawn through the apparatus 5 inches at a time, held stationary for the period of exposure, and moved on again During the stationary period the film is held at rest by two punches which perforate it on either margin, the exposure area beneath the aluminium window is compressed between intensifying screens, and an electrical contact, which indirectly operates the X-ray tube, is closed

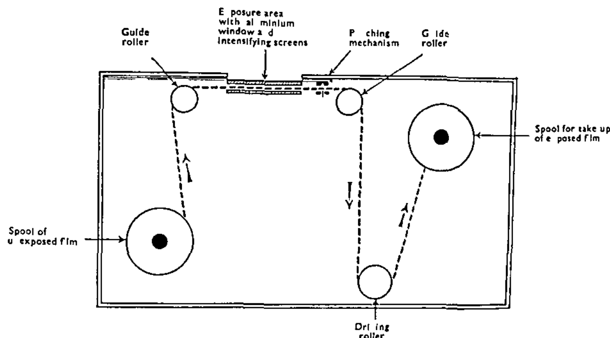


FIG 11 —Diagram of the direct cineradiographic camera showing how the X ray film passes through the apparatus

The camera speed is limited by two factors, a mechanical and an electrical one To obtain a film which can be projected at normal speed, exposures must be made at the rate of 16 frames per second, and the mechanical difficulty of moving and bringing to rest a large film, and releasing and compressing the intensifying screens, at a rate which allows of these exposures is obvious The electrical problem lies in the difficulty of interrupting the current at such short intervals, as the usual forms of contactor are necessarily built to carry heavy currents and are consequently too cumbrous for rapid operation The apparatus used at the Nuffield Institute was designed to operate at a maximum rate of 8 frames per second, but owing to the weight of the moving parts and the consequent vibration this high speed is not advisable for routine use, and the maximum recording rate employed as yet has been 3 to 4 frames per second, this has, however, proved adequate for the object of our immediate studies

While the films recorded by this method at a rate of 3 to 4 frames per second cannot be considered as cinematographic films in the generally accepted sense of the term, and are primarily intended for direct viewing, they can be transferred to 16 mm film and projected in this form For this purpose, to repro-

duce the actual rate of movement, each frame of the direct film, when recorded at a speed of, say, 3 frames per second, must be reproduced on 5 frames of the 16 mm film, thus producing a rate approximately equivalent to 16 frames per second, which is the normal speed in projection Films produced and projected in this way depict all movements with a slight jerkiness, but they are sometimes useful for demonstration purposes, as they give a visual impression of the altering forms and changing positions that can otherwise be deduced only by comparison of tracings made from individual frames of the direct film

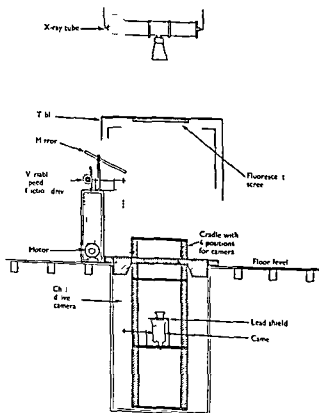


Fig 12 —Diagram to illustrate the principles of the indirect cineradiographic apparatus

The indirect method —The Nuffield Institute was originally equipped with the apparatus for indirect cineradiography designed by Dr Russell Reynolds (Reynolds 1936) This apparatus with its vertical fluorescent screen, was impractical for our studies of the circulation and particularly for our foetal work, in which, for operative reasons, a horizontal screen was required Attempts to adapt the existing apparatus to meet our special needs were unsuccessful, and accordingly a set up was assembled for recording subjects in the necessary horizontal position This apparatus did not include the elaborate synchronizing mechanism of the Russell Reynolds set, but never-

theless the films obtained proved to be adequate for our research purposes[1]

Fig 12 illustrates the principles of this apparatus in diagrammatic form The X-ray tube is directed vertically downwards over a table, which is secured to a fixed position on the floor On the under surface of the table is fixed a fluorescent screen Directly below the screen a pit in the floor, 3 feet in depth, houses a cradle which supports a 16 mm cinema camera facing vertically upwards The cradle is fitted with four positions for the camera, at various levels (i e distances from the fluorescent screen), according to the size of the field to be photographed The camera, which has an f/0 85 lens, is operated by a chain drive, transmitted from a separate unit which stands on the floor beside the pit This unit also carries a mirror for viewing the fluorescent screen

The camera speed normally employed in our circulation studies is 25 frames per second,[2] and the films thus obtained, when projected at a rate of 16 frames per second, give a slow motion effect of about 35 per cent

The above account has been confined to a bare outline of the radiographic techniques employed, and gives little idea of the complexities of the two sets of apparatus or of the practical difficulties involved in their use in research Both the direct and the indirect methods have their special indications, for each method has its own merits and limitations The direct method has the outstanding advantage that it provides the sharply defined, life-size pictures for direct viewing that are essential for accurate investigation and analysis On the other hand, for technical reasons it is as yet impracticable for films to be recorded by this method at the rapid speed that can be used as routine with the indirect method Since only low X-ray factors are required for the periodic exposure of each frame, the load on the X-ray tube is comparatively slight and thus, for practical purposes, no limit has to be set on this account to the length of a given record The high cost of the large film, however, constitutes a disadvantage of this method, although this has proved less than was anticipated, for experience has shown that by careful arrangement and timing the required record can generally be obtained on a comparatively short length of film

The great value of the indirect method lies in the fact that movements can be recorded and projected at their actual speed or even in slow motion Against this, however, has to be set the relatively poor quality of the picture obtained, which cannot be compared in the matter of definition and detail with that of the direct film Moreover, notwithstanding the great increase in the sensitivity of photographic films in recent years, high X-ray factors are still required to provide sufficient illumination of the fluorescent screen, and consequently each record must be strictly limited to a period of only a few seconds' duration in order to avoid undue load on the X-ray tube

[1] The design of this apparatus which is of simple home made construction has certain inherent faults which make it impossible to obtain absolute and consistent uniformity of exposure and the consequent slight fluctuation in the density of the films while not seriously interfering with their research value admittedly detracts from their technical quality To surmount this difficulty the apparatus is in process of reconstruction

[2] The camera speed is determined by the frequency of the electrical supply (50 cycles) to which it must bear an exact relation if uniformity of exposure is to be obtained

It will thus be seen that the method used for any given experiment is determined in each case by the nature of the record required In our studies of the foetal circulation it was essential primarily to obtain films that could be subjected to detailed analysis, and since the direct method, when operated at a rate of 3 to 4 frames per second was found to be sufficiently rapid to demonstrate the main features of the blood flow, the majority of our records were made with the use of this technique To supplement these records, however the indirect method was used to make films which could be projected and viewed as a genuine motion picture In addition the films recorded by the indirect method, when used in conjunction with lipiodol, permitted a frame-by-frame analysis of the path of individual globules that was sufficiently detailed for the construction of diagrams of the course of the blood flow, such as those reproduced in figs 19 and 32

Time recording apparatus—In our foetal circulation experiments it was essential to have accurate records of the time relations of various procedures For this purpose an apparatus was devised for registering all the necessary information on a kymograph tracing Six writing levers (made in the Institute at trifling cost) are available The first of these, connected to a time marker, records time intervals and the second which is connected to a contact on the camera drive of whichever apparatus is in operation automatically registers the exposures The remaining four levers are connected to switches on a control panel which are operated by hand for recording injections, the division of the umbilical cord the removal of the nose bag etc In our somewhat complicated experiments this simple but effective apparatus has automatically timed the cineradiographic records and has made it possible to correlate them accurately with other procedures

(ii) DEMONSTRATION AND DESCRIPTION OF FINDINGS

For some years past the vessels of the peripheral cardiovascular system have been rendered opaque to X-rays in the living subject by the use of contrast media circulating in the blood, but the application of this technique to demonstrate the course of the blood stream through the heart is of very recent origin The technique has been rendered practicable only by the development of non-toxic radio opaque media and by the introduction of cineradiography, and, so far as we are aware it has never before been applied, or at least successfully applied to a study of the foetal circulation

Our radiographic records of the foetal blood flow belong to two main groups (1) those demonstrating the circulation through the heart and great vessels, and (2) those demonstrating the circulation through the liver

The interpretation of the shadows recorded is not a simple matter An X ray picture is not a photograph It gives no hint of the depth at which the substance that causes the shadow lies Substances lying at various depths in the path of the rays cause shadows that are superimposed, and the disentanglement of a composite shadow into its various component parts may present considerable difficulty For instance, in the case of the heart and the vessels connected with it even the lateral radiograph which we have found to be the most satisfactory projection, presents a number of complex shadows of super-

imposed structures In order to help the reader to a better understanding of the radiographs reproduced in this chapter, some simple diagrams are given These diagrams, which have been constructed from tracings of actual radiographs, do not pretend to accuracy in detail, but illustrate the general course of the blood flow, as demonstrated in our various records, and show in particular the relations in this projection of the right and left sides of the heart and of the respective vessels by which they receive and discharge the blood It will be noted that no distinction is made between atrium and ventricle, in the radiographic records the line of demarcation between these two chambers is frequently indiscernible, particularly on the left side, and in any case its position changes with pulsation, although the general contour of the heart alters little (see Chapter IV)

In the following account an attempt is made to present the broad outline of our records in the simplest form we can attain, i e by the illustration and description of typical results, arranged in the order which experience has shown that they are most easily appreciated The course of the blood flow through the heart is more complex in the foetus than it is in the adult, and for this reason the adult circulation is briefly demonstrated first, so that the reader may pass more readily to the study of the foetal circulation, with which he is probably less well acquainted It is hoped that by this arrangement the reader who is unfamiliar with the interpretation of radiographs or with the details of the foetal circulation will be able to obtain an insight into the groundwork that underlies the subsequent Chapters, in which (contrary to the order adopted in this section) the material is arranged to follow the logical sequence of the course of the blood flow

The Circulation through the Heart and Great Vessels

The circulation through the heart is demonstrated in its two main aspects (1) the course of flow of the blood entering the heart from the *superior/anterior vena cava*,[1] as shown by contrast medium injected into the external jugular vein (anterior caval injection), and (2) the course of flow of the blood entering the heart from the *inferior/posterior vena cava*,[1] as shown by contrast medium injected either into the umbilical vein or into the femoral vein (posterior caval injection)

ADULT[2] CIRCULATION

(*Figs 13a and 13b*) In the adult, venous blood entering the heart, both from the anterior vena cava (*1a*) and from the posterior vena cava (*1b*), flows through the right side of the heart (2) After passing through the right atrium and right ventricle it leaves the heart by the pulmonary valve and pulmonary trunk (3), and flows along the pulmonary arteries (4) to the lungs

[1] In the case of pronograde animals the terms anterior and posterior are commonly used in connection with the two venae cavae being more appropriate than the corresponding terms superior and inferior applied to these vessels in the human subject

[2] As the radiographic records are concerned with the circulatory apparatus alone the meaning of the term adult (so far as the flow through the heart is concerned) has been extended to connote any animal in which the ductus arteriosus and the foramen ovale have ceased to function as blood channels

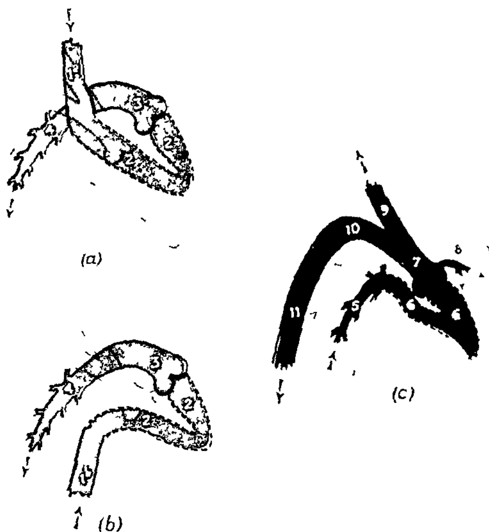


Fig 13

(*Fig* 13*c*) After being re oxygenated in its passage through the lung capillaries the blood returns along the pulmonary veins (5) to the left side of the heart (6) passing through the left atrium, the left ventricle and aortic valve to enter the ascending aorta (7) Some of the blood is now distributed to the heart muscle itself via the coronary arteries (8), and to the anterior part of the body via the brachiocephalic artery [1] (9) while the remainder passes round the aortic arch (10) to the descending aorta (11) to be distributed to the rest of the body

[1] In the sheep (from which the diagrams are constructed) as in many other lower mammals only one trunk the brachiocephalic artery arises from the arch of the aorta This single trunk corresponds to the innominate left common carotid and left subclavian arteries of Man In the cat (Plate I and figs 14 and 15) two trunks arise from the aortic arch namely the innominate and the left subclavian arteries

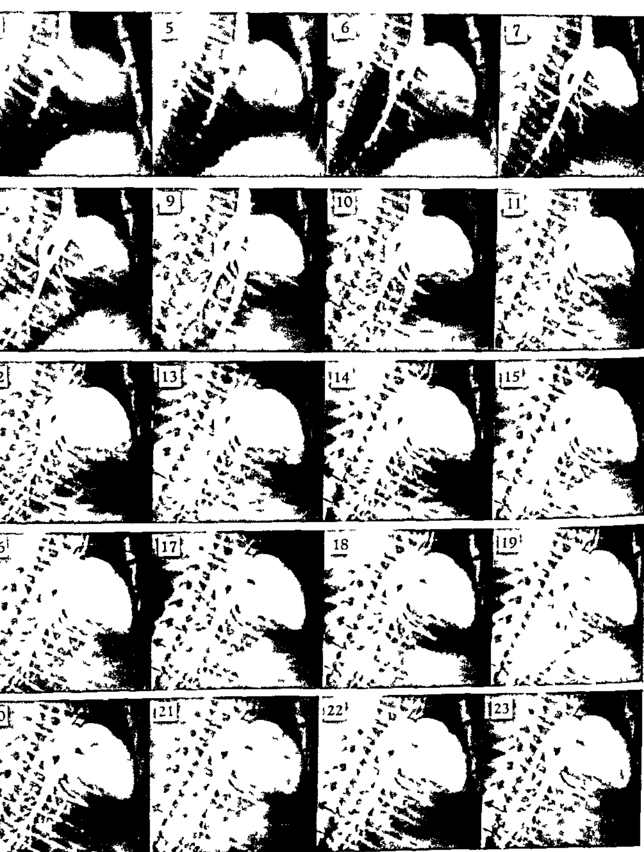
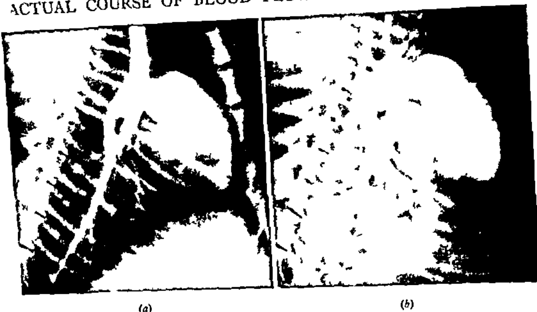


PLATE I.—Cat, adult. Part of a direct cineradiographic record (made at the rate of 3 frames per second) of a jugular n injection demonstrating the course of the anterior caval flow through the heart and great vessels. See fig. 14.



(*a*) (*b*)

FIG 14 —Cat adult Frames 6 and 23 of record figured in Plate I

Contrast medium passing (*a*) from the anterior vena cava through the right heart pulmonary trunk and pulmonary arteries to the lungs and (*b*) returning from the lungs by the pulmonary veins to the left heart and passing to the aorta and its branches

Plate I, in which are reproduced 20 consecutive frames of a direct cineradiographic record made of an injection of contrast medium into the jugular vein of a cat, demonstrates the course of the anterior caval flow through the heart and great vessels in the adult The passage of the contrast medium first through the right heart and pulmonary arteries to the lungs and later, its return from the lungs along the pulmonary veins to the left heart and the arterial vessels supplied therefrom may be more clearly seen in fig 14, in which frames 6 and 23 of this record are reproduced on a larger scale (In Plate I it will be noted that at one stage of the injection the contrast medium momentarily passes out of the right atrium down into the posterior vena cava, and even enters some of the hepatic veins This was probably due in part to a too rapid injection and in part to the fact that the contrast medium used in this case was sodium iodide which has a *toxic effect on the heart* On the other hand retrograde movements of blood in the thoracic posterior vena cava of the adult are not necessarily abnormal—see Franklin, 1937, 291)

Fig 15 frames taken from a similar record of an injection of contrast medium into the femoral vein of a cat shows two stages in the course of the posterior caval flow

FOETAL CIRCULATION

Bearing in mind the course of the circulation through the heart of the adult and its radiographic demonstration, we turn now to the foetal circulation In the foetus the blood is re oxygenated not in the lungs but in the placenta, and



(a) (b)

FIG 15 —Cat adult Frames from a record of a posterior caval injection

Contrast medium passing (a) from the posterior vena cava through the right heart pulmonary trunk and pulmonary arteries to the lungs and (b) returning from the lungs by the pulmonary veins to the left heart and passing to the aorta and its branches

two by-passes are provided which short-circuit the pulmonary system the ductus arteriosus, and the so-called " foramen ovale "[1] As will be seen below, the ductus arteriosus enables much of the venous blood entering the heart from the anterior vena cava to pass directly to the descending aorta (and thence to the placenta) without traversing the lungs, while the " foramen ovale " allows the greater part of the blood from the posterior vena cava (including the re-oxygenated blood from the placenta) to pass immediately to the left side of the heart and thus directly to the ascending aorta and the vessels which it supplies

As has already been indicated, in order to obtain a reliable picture of the strictly foetal circulation, the first records of nearly all the experiments were made under conditions approximating as nearly as possible to those of the intra-uterine existence of the foetus, i e with the placental circulation continuing through the umbilical cord, and with respiration prevented by means of a rubber nose-bag, filled with amniotic fluid, covering the muzzle of the foetus Later in each experiment, or occasionally from the beginning, the nose-bag was removed to allow respiration to begin and the umbilical cord was divided between ligatures, so that records could be obtained of the changes in the circulation that take place at or shortly after birth

[1] Lest the reader should be confused by the introduction at this stage of unfamiliar terminology the term foramen ovale is adhered to throughout this Chapter To the use of this term however there are certain objections (see page 86) and the authors revised nomenclature for this and various other structures concerned in the foetal circulation is adopted in subsequent Chapters

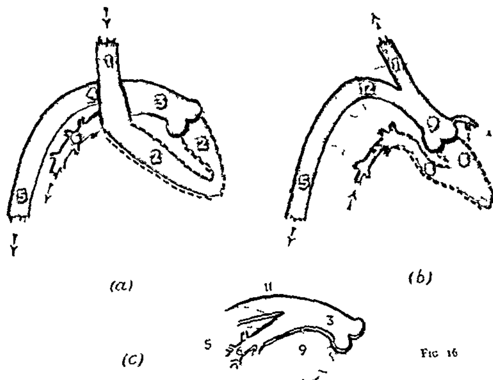


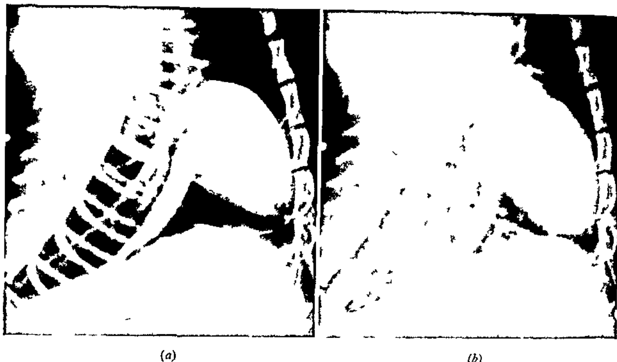
Fig 16

Anterior Caval Flow

(*Fig* 16*a*) The blood entering the heart from the anterior vena cava (1) (venous blood) passes in its entirety through the right side of the heart (2) and through the pulmonary valve to the pulmonary trunk (3) Thus far the anterior caval blood of the foetus follows the same course as that of the adult but beyond this point a difference is at once apparent While some of the blood passes along the pulmonary arteries (6) to be distributed to the lungs as in the adult, a large quantity is also carried via the ductus arteriosus (4) directly into the descending aorta (5), and thence by the aorta's two large terminal branches, the umbilical arteries to the placenta

(*Fig* 16*b*) In the foetus the lungs are not concerned with respiration, and the blood which traverses the lung capillaries does not become re oxygenated as in the adult The course however, taken by the blood returning from the lungs is the same as that in the adult, namely, it passes along the pulmonary veins (7) to the left side of the heart (8) and thence through the aortic valve to the ascending aorta (9) From here some is distributed to the coronary (10) and brachiocephalic (11) arteries, while the remainder passes round the aortic arch (12) to the descending aorta (5)

Fig 16*c* obtained by superimposition of figs 16*a* and 16*b* shows the arterial vessels leaving the right and left sides of the heart respectively, and the approximate relation of the ductus arteriosus to these vessels The exact site and radiographic appearance of the ductus are discussed below



(a) (b)

Fig 15 —Cat adult Frames from a record of a posterior caval injection

Contrast medium passing (a) from the posterior vena cava through the right heart pulmonary trunk and pulmonary arteries to the lungs and (b) returning from the lungs by the pulmonary veins to the left heart and passing to the aorta and its branches

two by-passes are provided which short-circuit the pulmonary system the ductus arteriosus, and the so-called " foramen ovale "[1] As will be seen below, the ductus arteriosus enables much of the venous blood entering the heart from the anterior vena cava to pass directly to the descending aorta (and thence to the placenta) without traversing the lungs, while the 'foramen ovale" allows the greater part of the blood from the posterior vena cava (including the re-oxygenated blood from the placenta) to pass immediately to the left side of the heart and thus directly to the ascending aorta and the vessels which it supplies

As has already been indicated, in order to obtain a reliable picture of the strictly foetal circulation, the first records of nearly all the experiments were made under conditions approximating as nearly as possible to those of the intra-uterine existence of the foetus, i e with the placental circulation continuing through the umbilical cord, and with respiration prevented by means of a rubber nose-bag, filled with amniotic fluid, covering the muzzle of the foetus Later in each experiment, or occasionally from the beginning, the nose-bag was removed to allow respiration to begin and the umbilical cord was divided between ligatures, so that records could be obtained of the changes in the circulation that take place at or shortly after birth

[1] Lest the reader should be confused by the introduction at this stage of unfamiliar terminology the term foramen ovale is adhered to throughout this Chapter To the use of this term however there are certain objections (see page 86) and the authors revised nomenclature for this and various other structures concerned in the foetal circulation is adopted in subsequent Chapters

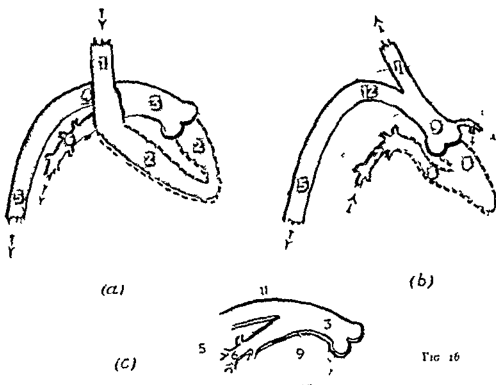


Fig 16

Anterior Caval Flow

(*Fig* 16*a*) The blood entering the heart from the anterior vena cava (1) (venous blood) passes in its entirety through the right side of the heart (2) and through the pulmonary valve to the pulmonary trunk (3) Thus far the anterior caval blood of the foetus follows the same course as that of the adult, but beyond this point a difference is at once apparent While some of the blood passes along the pulmonary arteries (6) to be distributed to the lungs, as in the adult a large quantity is also carried via the ductus arteriosus (4) directly into the descending aorta (5), and thence by the aorta s two large terminal branches, the umbilical arteries to the placenta

(*Fig* 16*b*) In the foetus the lungs are not concerned with respiration, and the blood which traverses the lung capillaries does not become re oxygenated as in the adult The course, however, taken by the blood returning from the lungs is the same as that in the adult namely, it passes along the pulmonary veins (7) to the left side of the heart (8), and thence through the aortic valve to the ascending aorta (9) From here some is distributed to the coronary (10) and brachiocephalic (11) arteries while the remainder passes round the aortic arch (12) to the descending aorta (5)

Fig 16*c* obtained by superimposition of figs 16*a* and 16*b*, shows the arterial vessels leaving the right and left sides of the heart respectively and the approximate relation of the ductus arteriosus to these vessels The exact site and radiographic appearance of the ductus are discussed below

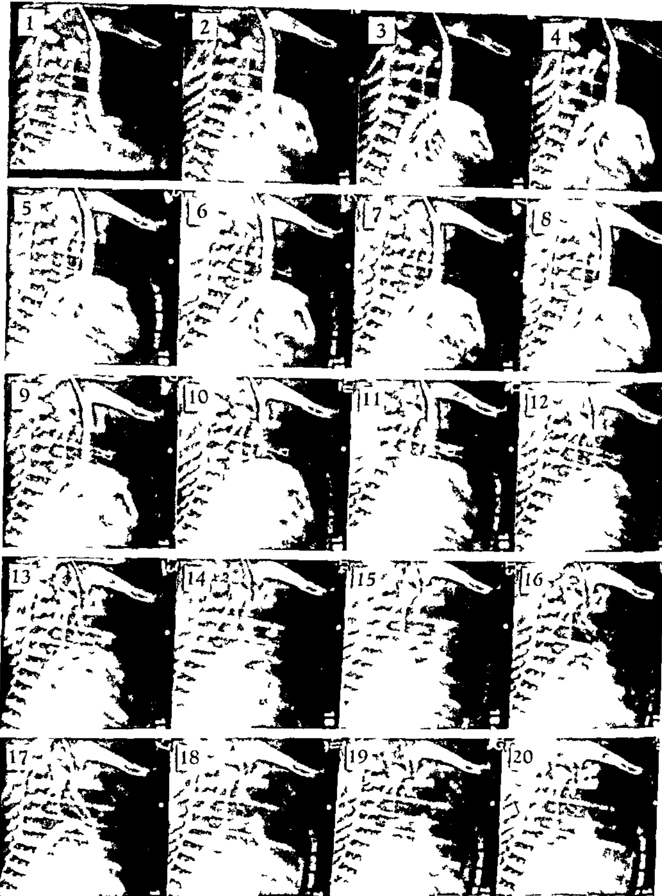


PLATE II.—Sheep foetus (118/147 days). Nose bag on; cord undivided. Part of a direct cineradiographic record (made at the rate of 3 frames per second) of a jugular vein injection demonstrating the course of the anterior caval flow through the heart and great vessels. See fig. 17.



(a) (b)

Fig 17.—Sheep foetus (118 147 days) Nose bag on Cord undivided Frames 6 and 16 of record figured in Plate II

(a) Contrast medium passing from the anterior vena cava through the right heart to the pulmonary trunk and thence both via the ductus arteriosus to the descending aorta and along the pulmonary arteries to the lungs

(b) The right heart is now empty and that portion of the contrast medium which earlier passed along the pulmonary arteries to the lungs is returning from the lungs by the pulmonary veins to the left heart and filling the ascending aorta brachiocephalic artery aortic arch and descending aorta

(a) (b)

Fig 18.—Sheep foetus (100 147 days) Nose bag on Cord undivided

Frames from a record of an anterior caval injection showing (a) its passage through the right heart to the pulmonary trunk and thence both via the ductus arteriosus to the descending aorta and along the pulmonary arteries to the lungs (b) the return flow from the lungs by the pulmonary veins to the left heart and its passage thence to the ascending aorta and its branches

F C—4

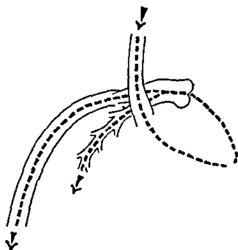


Fig 19—Diagram constructed from a frame by frame analysis of an indirect cineradiographic film showing the course through the heart and great vessels taken by globules of lipiodol injected into the jugular vein of a sheep foetus It will be seen that the course is similar to that taken by the miscible contrast media in figs 17*a* and 18*a*

Typical records demonstrating the course of the foetal anterior caval flow are reproduced in Plate II, and in figs 17, 18, and 19

The fact that the whole of the anterior caval flow passes through the right heart is indicated partly by the location of the shadow of the opacified blood within the area of the heart itself, but still more conclusively by the absence of any shadow in the arterial vessels which are supplied from the left side of the heart In this respect the brachiocephalic artery forms a useful criterion, for when this vessel receives opacified blood its shadow can be clearly distinguished from that of other structures If any part of an injection of contrast medium entering the heart by the anterior vena cava were to pass through the left side of the heart, a shadow would immediately be seen in the brachiocephalic artery In our records of such injections, however, no shadow is ever seen in this vessel until after the opaque blood has returned to the left heart by the pulmonary veins (after making the pulmonary circuit) or from elsewhere[1]

The ductus arteriosus —In our first season's work (Barclay, Barcroft, Barron, and Franklin, 1938, c) we identified the ductus arteriosus in our radiographic records as a vessel of fine calibre, the shadow of which apparently formed a junction between that of the pulmonary arterial system and that of the aorta Further experience in interpretation of the records and improvements in experimental techniques soon showed the fallacy of our initial observations and made it clear that the shadow which we had originally described as that of the ductus arteriosus in fact depicted a branch of one of the pulmonary arteries In view of the difficulties which we ourselves experienced in our early work, it seems worth while to discuss in some detail the site and radiographic appearance of the ductus arteriosus, which, as will be seen in fig 20, is a vessel of considerable size, approximating to that of the aorta itself

Our initial mistake was due for the most part, it must be frankly admitted, to an improper approach to the investigation We were attempting to solve a question of specific detail without first arriving at a full understanding of the whole picture On the other hand, certain mistakes or deficiencies in our experimental techniques made the radiographs of what was at that time a wholly unfamiliar subject still more difficult to interpret In the first place, we

[1] It occasionally happens that a too rapid injection momentarily forces some of the contrast medium to pass out of the right atrium back into the posterior vena cava against the normal flow of blood in that vessel (instances of this may be seen in certain frames of Plate I and in figs 63 64) On returning again to the heart much of this backflow passes directly into and through the left side (see course of foetal posterior caval flow, pp 57–61) and a shadow then quickly appears in the brachiocephalic artery

had been using thorotrast as the contrast medium and this substance, as has already been stated, is not eliminated from the circulation in the sheep foetus in the same way as it is in the adult dog or cat Secondly we had injected a considerable quantity (20 c c or more) at a time introducing it fairly slowly Thirdly, in order to obtain continuous records over as long a period as possible with the limited lengths of film available, the speed of recording did not exceed one frame per second and was often slower than this The combined effect of these three factors was that with the possible chance exception of a single initial frame or so the radiographic records showed the whole of the cardiovascular system filled with contrast medium in greater or less degree Even a repeat injection could seldom be clearly distinguished from the persisting shadow of the previous one



FIG 20—Photograph of the exposed heart and great vessels of a sheep foetus showing the relations of the ductus arteriosus (here partly contracted down) The left side of the chest part of the left lung and part of the pericardium have been removed (Photograph taken from the left side and reversed here to correspond with the radiographic projection cf fig 66) *R V* right ventricle *L V* left ventricle *P T* pulmonary trunk *P A* left pulmonary artery *D* ductus arteriosus *D A* descending aorta *A* aortic arch *B C A* brachiocephalic artery Scale in cm

When the chambers of the heart and the vessels connected with it are all filled with contrast medium, the ductus arteriosus is almost entirely merged in a complex shadow derived from the following structures anterior vena cava right atrium pulmonary trunk, descending aorta aortic arch, root of brachiocephalic artery and possibly some pulmonary arterial vessels Even in a stage where the contrast medium is still confined to the right heart and the vessels connected with it, it is often difficult to distinguish the ductus as an individual vessel, for the shadow may extend with its contour apparently unbroken from the pulmonary trunk to the descending aorta (see e g, fig 21*a*)

Two types of experiment suggested themselves as a means of locating on the radiographic records the exact site of the ductus In the first, we would affix an identifying mark to the actual vessel before making an injection of contrast medium In the second we would inject fairly quickly only a small quantity of contrast medium which would pass through the cardiovascular system en masse showing the various vessels and chambers of the heart in succession For both types of experiment, the records of which were required to cover only a short period of time the speed of recording would be increased to 3 frames per second

An experiment of the first type is illustrated in fig 21 After a preliminary injection had been recorded in its passage through the heart from the anterior vena cava (fig 21*a*), the thorax of the foetus was quickly opened on the left side

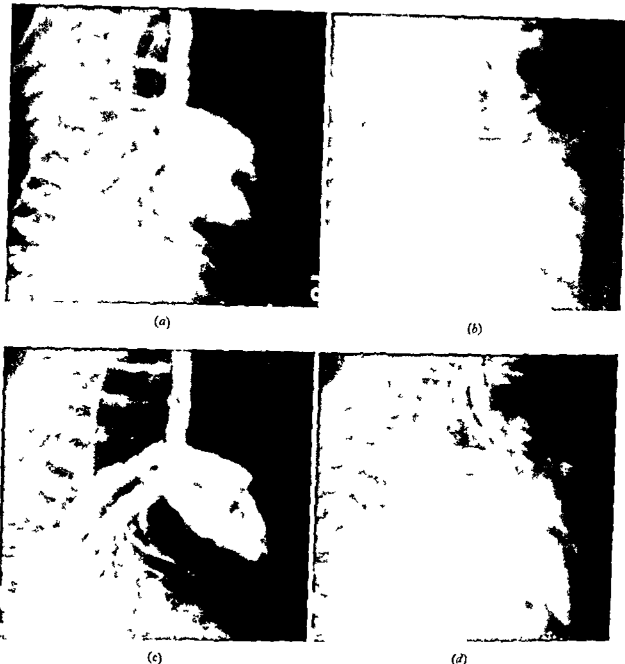


Fig 21—Sheep foetus (118 147 days) Nose bag on Cord undivided

(a) Preliminary anterior caval injection

(b) The thorax has been opened and a piece of wire sewn on to the ductus arteriosus The contrast medium injected previously still faintly outlines the vessels

(c) A second anterior caval injection shows the relation of the wire on the ductus to the anterior vena cava the pulmonary trunk the pulmonary arteries and the descending aorta

(d) Four seconds later the injection shown in (c) is seen to have passed on from the right heart and to be returning from the lungs along the pulmonary veins to the left heart passing thence through the aortic valve to the ascending aorta and the vessels supplied therefrom Note the relation of the wire on the ductus to *the aortic arch* and *compare the sharp bend of this arch with the much more gradual curve formed by the* pulmonary trunk ductus arteriosus and descending aorta in (a) and (c)

and a piece of wire of approximately the same length as the ductus was sewn on to this vessel The thorax was then closed, and fig 21*b* shows the wire in position It will be noted that the contrast medium previously injected

has not yet been entirely eliminated and still faintly outlines the vessels A second injection was then made (fig 21*c*) It will be seen that the wire is almost lost in the general shadow and that it lies at right angles to the anterior vena cava (It is of interest to note that the opening of the thorax has not seriously disturbed the anatomical picture, cf fig 21*a*) In fig 21*d*, four seconds later the contrast medium has been largely cleared from the right heart and the vessels connected with it and is seen returning from the lungs along the pulmonary veins to the left heart and passing to the ascending aorta and the vessels supplied therefrom The relation of the wire on the ductus to the aortic arch is well seen



Fig 22 —Sheep foetus (nearly full term) Frame from a record of an anterior caval injection in which the relation of the ductus arteriosus to the pulmonary trunk the pulmonary arteries and the descending aorta is more clearly seen owing to the absence of contrast medium in the anterior vena cava and the vessels connected with the left heart (see text)

Fig 22 is taken from a record of the second type of experiment The contrast medium has just passed on from the anterior vena cava leaving this vessel almost empty, and is filling the right heart and the vessels leading from it, but it has not yet reached any of the vessels connected with the left side of the heart The course of the ductus as it branches from the pulmonary trunk is well seen but its exact point of origin and its anastomosis with the descending aorta cannot be accurately determined The slight break in the natural curve of the aorta indicates the approximate site of the anastomosis

As a result of these experiments the site of the ductus in our radiographic records was determined fairly accurately, but in addition its position and relation to the neighbouring vessels was indisputably demonstrated by a purely fortuitous experiment In this experiment the story of which is told in another Chapter, an injection of contrast medium was unintentionally made into the femoral artery instead of into the femoral vein Owing to the very feeble action of the heart, the injection passed up the aorta as far as the heart itself which it was unable to enter by reason of the aortic and pulmonary valves Thus we obtained a record of successive stages in a retrograde filling of the arterial systems leading from the two sides of the heart including the ductus arteriosus without the complication of shadows in the heart itself and in the veins entering it This record is figured in Plate III, and a single frame from the latter part is reproduced in fig 23 Here a feeble pulsation of the left heart has momentarily cleared the ascending aorta and partially cleared the brachiocephalic artery and aortic arch leaving a well defined picture of the

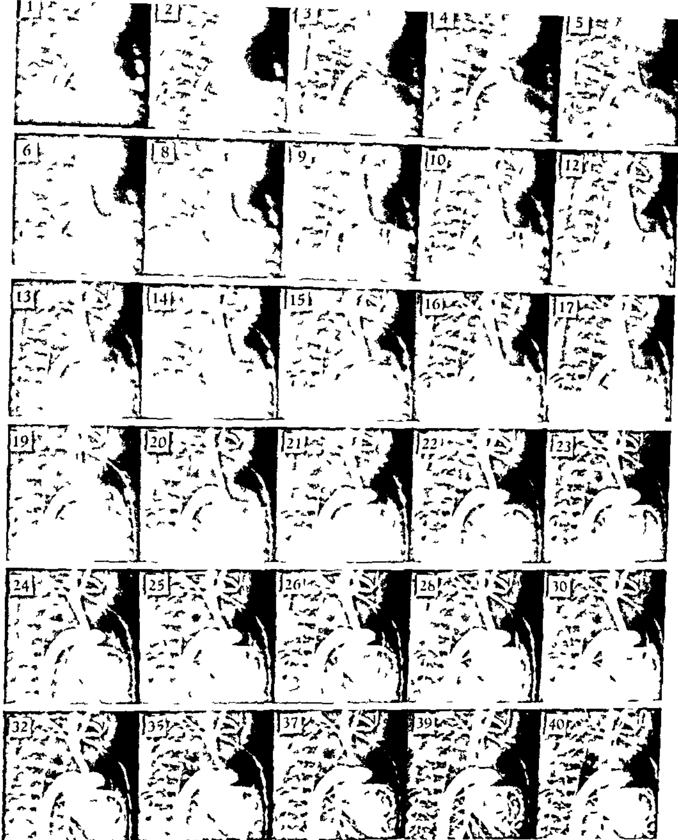


Plate III —Sheep foetus (*c* 100/147 days) No nose bag cord divided Selected frames of a direct cineradiographic record (made at the rate of 3 frames per second) of a retrograde intra arterial (femoral artery) injection The contrast medium is seen passing up the descending aorta and filling in succession the aortic arch the ascending aorta the brachiocephalic and coronary arteries the ductus arteriosus the pulmonary trunk and pulmonary arteries The foetus was in very poor condition at the time of injection its heart beating only feebly and from time to time *See text (p 53) and fig 23*

ductus uniting the pulmonary trunk and descending aorta



FIG 23 —Sheep foetus (*c* 100/147 days) Frame 39 of record figured in Plate III (retrograde intra arterial injection) A feeble pulsation of the left heart has momentarily cleared the ascending aorta and partially cleared the aortic arch and brachiocephalic artery thus leaving a well-defined picture of the ductus arterio us uniting the pulmonary trunk and the descending aorta

The Change in the Course of the Anterior Caval Flow after Functional Closure of the Ductus Arteriosus

While the methods described above afford an *anatomical* identification of the ductus arteriosus, the patency or closed state of the vessel can be determined by observing the course taken by the blood on leaving the right heart, i e by a *functional* test Under foetal conditions, blood reaching the descending aorta may come from one or other of two sources (see fig 16*c*) either from the right heart, via the pulmonary trunk and ductus arteriosus, or from the left heart via the ascending aorta and aortic arch Since as has been shown, the anterior caval flow passes in its entirety through the right heart the appearance of contrast medium in the descending aorta, immediately following an anterior caval injection, indicates that the ductus arteriosus is patent for it can only have come through this channel If on the other hand, no such shadow appears and the contrast medium passes exclusively to the pulmonary arteries, the ductus arteriosus may be considered to be functionally closed

Figs 24 and 25 are taken from two experiments of a group designed to record the transition from the stage when the ductus is patent to that when it is functionally closed, and so to determine the time of closure For this series of experiments the contrast medium used was one of those that are quickly eliminated from the blood and small injections (4–7 c c) were made and recorded at short intervals for as long a period as possible, sometimes up to two hours from delivery of the foetus In figs 24*a* and 25*a* the anterior caval injection is seen passing freely to the descending aorta as well as to the pulmonary arteries while in figs 24*b* and 25*b*, taken from later records of the same two animals, a similar injection is passing only to the pulmonary arteries In each case during the interval between the two injections the ductus had ceased to be a functioning vessel

In a number of our records a pointed stub may be seen projecting from the pulmonary trunk at the site of origin of the ductus This appears to be the blind end of the functionally closed vessel The stub is shown in fig 26*a*, but in fig 26*b* (about 2 seconds later in the same record), which demonstrates



(a) FIG 24 —Sheep foetus (144/147 days) (b)

(a) Anterior caval injection 6½ minutes from delivery Nose bag on cord undivided The contrast medium is passing freely through the ductus arteriosus to the descending aorta as well as to the pulmonary arteries

(b) Another anterior caval injection 4½ minutes later The nose bag had been removed and the cord divided 4 minutes before this injection The contrast medium is now passing to the pulmonary arteries only and no shadow is seen in the descending aorta i e the ductus arteriosus is functionally closed



(a) (b)

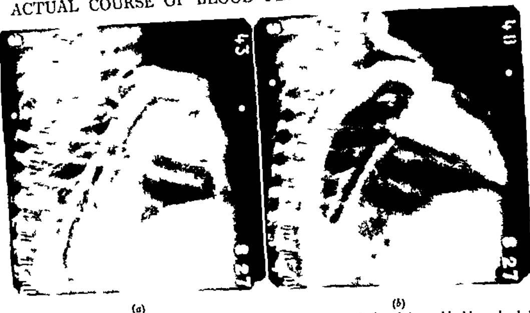
FIG 25 —Sheep foetus (nearly full term) No nose bag had been applied and the cord had been divided on delivery

(a) Anterior caval injection 3 minutes from delivery The course taken by the contrast medium shows that the ductus arteriosus is patent

(b) Another anterior caval injection 8 minutes later shows that the ductus is functionally closed

the return flow from the lungs to the left heart and the filling of the arterial vessels supplied from this side of the heart, it will be noted that the right heart is devoid of any shadow and that the stub is no longer seen, i e there is no suggestion that any of the opacified blood in the descending aorta is passing back through the ductus

The functional closure of the ductus arteriosus is not always as complete and final as might be inferred from the examples that have been quoted, and in



(a) (b)

FIG 26 —Sheep foetus (nearly full term) No nose bag had been applied and the cord had been divided on delivery 32 minutes before this record

(a) Contrast medium of an anterior caval injection is seen filling the pulmonary trunk and pulmonary arteries Note the pointed stub springing from the pulmonary trunk at the site of origin of the ductus The ductus is functionally closed and allows no contrast medium to pass to the descending aorta

(b) 1½ seconds later the right heart is empty and the contrast medium is seen returning from the lungs along the pulmonary veins to the left heart and the vessels which it supplies There is no indication of any backflow from the descending aorta through the ductus arteriosus to the pulmonary trunk

some cases the channel having once closed has opened again When, however such a reopening occurred it appeared to be associated with a general deterioration in the condition of the foetus, and our records indicate that in the case of a healthy, vigorous animal functional closure of the ductus arteriosus occurs very shortly (within 5 minutes in one case) after the foetus has assumed its independent existence

Posterior Caval Flow

Our radiographic records demonstrate the course of flow through the heart of two of the main components of the posterior caval blood stream namely, the re oxygenated blood which returns to the foetus from the placenta and the venous blood which returns to the heart from the lower segment of the body, i e from the abdominal vena cava The distribution of the blood from these two sources was determined by recording the course taken by contrast medium injected into one of the umbilical veins within the cord and into the femoral vein respectively [1]

[1] Records of miscible contrast medium injected into the umbilical or femoral vein to show the course of the posterior caval flow through the heart have often been lacking in clarity While the reasons for this are not yet wholly apparent certain contributory factors can be appreciated First in both cases the site of injection is at some distance from the heart and so the contrast medium is progressively diluted by the various streams of normal (non-opaque) blood which join it in the course of its flow Secondly the rate of flow in the thoracic portion of the posterior vena cava itself appears from our records to be relatively low One of the factors contributing to this low rate of flow may be the presence of a caval band (see Franklin 1937 p 39) tending to restrict the flow through the posterior vena cava at the level of the diaphragm Many of our records (see e g fig 33) suggest that such a band is functioning but we cannot at present say more than that

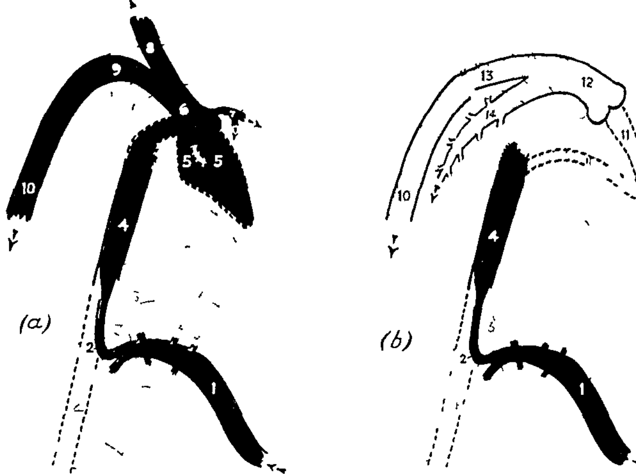


FIG 27

Flow from the Placenta

(*Fig* 27) In the sheep foetus the re-oxygenated blood returning from the placenta flows through *the umbilical cord in two veins which, shortly after their* passage through the skin of the foetus, fuse into a single vessel The blood flows up this common umbilical vein (1) into the liver, and thereafter enters the posterior vena cava (4) directly, via the ductus venosus (2), and indirectly, after traversing part of the liver (*see pp* 63–64), by *certain hepatic veins* (3) On entering the posterior vena cava (where it is joined by the rest of the hepatic blood, i e the portal inflow, and by the venous flow returning from the more caudal parts of the body) the blood passes up to the heart, here the stream divides

(*Fig* 27*a*) The greater part of the flow passes directly through the "foramen ovale" to the left side of the heart (5), and thence through the aortic valve to the ascending aorta (6) Some of the blood is now distributed to the coronary (7) and brachiocephalic (8) arteries, while the remainder passes round the aortic arch (9) to the descending aorta (10)

(*Fig* 27*b*) A smaller quantity passes into and through the right side of the heart (11), and thence through the pulmonary valve to the pulmonary trunk (12) Thereafter, it passes in part to the pulmonary arteries (14) and in part, via the ductus arteriosus (13), to the descending aorta (10) The terminal course, therefore, of this portion of the stream is the same as that of the anterior caval flow



PLATE IV —Sheep foetus (135/147 days) Nose bag on cord undivided Part of a direct cineradiographic cord (made at the rate of 3 frames per second) of an umbilical vein injection showing the course of flow through heart nd great vessels of that portion of the posterior caval blood which comes from the placenta See fig 28



(a) (b)

Fig 28 —Sheep foetus (135/147 days) Nose bag on Cord undivided Frames 4 and 7 of record figured in Plate IV

Contrast medium injected into one of the umbilical veins within the cord is seen passing up the thoracic posterior vena cava into the heart *Note in (a) the prompt appearance of a good shadow in the ascending* aorta brachiocephalic artery and aortic arch indicating a considerable flow through the foramen ovale and the left heart and in (b) 1 second after (a) the later appearance of a less pronounced shadow in the pulmonary arteries and ductus arteriosus indicating a much smaller flow through the right heart



(a) (b)

Fig 29 —Sheep foetus (140/147 days) Nose bag on Cord undivided Frames from a record of a femoral vein injection showing that the course of flow through the heart of the abdominal caval blood is similar to that of the blood returning to the heart from the placenta via the umbilical vein shown in fig 28 As in fig 28 the time interval between the two frames is 1 second

Plate IV and fig 28 are taken from records which demonstrate the passage through the heart of contrast medium injected into one of the umbilical veins within the cord It will be seen that a good shadow appears promptly (Pl IV

frame 4, fig. 28a) in the ascending aorta,[1] brachiocephalic artery and aortic arch indicating a considerable flow through the "foramen ovale" and the left heart, while a less dense shadow makes a later and more gradual appearance (Pl. IV, frame 5 onwards; fig. 28b) in the pulmonary arteries and ductus arteriosus indicating a much smaller flow through the right heart.



FIG. 30.—Sheep foetus (142/147 days). Frame from a record showing the "head" of a posterior caval injection dividing into two streams as it enters the heart. (The faint shadow in the vessels is due to a previous injection of contrast medium which has not been wholly eliminated.)

Flow from the Abdominal Vena Cava

As may be seen in fig. 29 the course of flow through the heart of the abdominal caval blood is similar to that of the blood returning from the placenta via the umbilical vein and ductus venosus shown in fig. 28. A good shadow appearing quickly in the ascending aorta, brachiocephalic artery and aortic arch serves as evidence that a considerable quantity of contrast medium has passed from the posterior vena cava through the "foramen ovale" and the left heart, while a much fainter and somewhat later appearing shadow in the pulmonary arteries and ductus arteriosus indicates that a relatively small quantity has passed through the right heart.

Owing to superimposed shadows it is seldom easy to differentiate the two portions of the posterior caval stream within the area of the heart itself, but the actual division of the stream as it enters the heart, is occasionally demonstrated in the records and may be seen in fig. 30. The anatomical basis for this division is discussed in Chapter III, but the reader may like at this point to study the photograph reproduced in fig. 31, in which the prominent ridge on which the posterior caval stream divides is clearly seen.

[1] In some frames (e.g. that shown in fig. 28b) one of the coronary arteries can just be discerned, but when miscible contrast media is used it is generally difficult to see the filling of these vessels owing to their small size and to the background of opacified blood within the chambers of the heart against which they lie. In many of the frames of the retrograde intra-arterial injection figured in Plate III, however, the coronary arteries are clearly seen, and their supply with blood from the left heart is well demonstrated by posterior caval injections of lipiodol (see fig. 3 a).



Fig 31 —Dorsal aspect of the heart and great vessels of a nearly full term sheep foetus dissected to show *inter alia* the marked ridge on which the posterior caval stream divides as it enters the heart (see also figs 49–54) Part of the dorsal wall of the posterior vena cava and the dorsal walls of the anterior vena cava and left atrium have been removed Scale in cm

The Change in the Course of the Posterior Caval Flow after Functional Closure of the "Foramen Ovale" and the Ductus Arteriosus

When, shortly after birth, the "foramen ovale" becomes functionally closed, the whole of the posterior caval flow takes the course followed by the smaller stream in the foetal stage, passing through the right heart to the pulmonary trunk (see fig 32*b*) From our records it appears that in the newborn lamb functional closure of the "foramen ovale" occurs before that of the ductus arteriosus, for when the contrast medium first takes this new, single course through the right heart, its shadow is seen still to pass from the pulmonary trunk through the ductus arteriosus to the descending aorta, as well as to the pulmonary arteries

The exact site of the "foramen ovale" in our radiographic records is often even more difficult to locate than that of the ductus arteriosus, but here again the patency or closed state of this foetal channel is readily determined by a functional test Just as the presence or absence of a shadow in the descending aorta, immediately following an anterior caval injection, indicates (as has already been shown) that the ductus arteriosus is patent or closed, so the patency or closed state of the "foramen ovale" is indicated by the presence or absence of a shadow in the brachiocephalic artery (or other vessels supplied exclusively from the left heart) immediately following a posterior caval injection

After functional closure of both the "foramen ovale" and the ductus arteriosus, the posterior caval flow passes in its entirety through the right heart to the pulmonary trunk and pulmonary arteries (figs 32*c* and 33), and the adult pattern of circulation through the heart and great vessels is established

The Circulation through the Liver in the Foetus

In one of our early experiments, designed to record the passage through the heart of contrast medium injected into one of the umbilical veins, the foetus was incorrectly positioned, with the result that the record obtained showed the flow of the injected contrast medium not through the heart, as intended, but in an earlier stage of its course, namely, through the liver The record thus accidentally obtained led in due course to an extension of our studies by an investigation into the circulation through the foetal liver, and a number of records were made to confirm and supplement observations which were in the first instance the result of an error in technique Owing to the lie of the

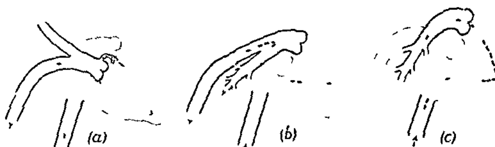


FIG 32—Diagrams constructed from a frame by frame analysis of indirect cineradiographic films recording injections of lipiodol showing the changes in the course of the posterior caval flow which take place after functional closure of the foramen ovale and ductus arteriosus

(a) *Foramen ovale patent*—This diagram depicts only the main course of the foetal posterior caval flow (i e that taken by the great majority of globules) through the left heart (cf fig 28 1) One or two globules (not shown here) passed through the right heart (Sheep foetus nearly full term No nose bag cord undivided Umbilical vein injection 3 minutes from delivery)

(b) "*Foramen ovale" functionally closed ductus arteriosus still patent*—A similar injection 2 minutes later in the same animal as that shown in (a)

(c) *Foramen ovale and ductus arteriosus both functionally closed*—Lamb a few weeks after birth Femoral vein injection

liver in the mature sheep foetus, wherein only a small portion of the viscus extends to the left of the dorso ventral midline, the hepatic circulation is best seen in the lateral projection

The blood supply of the foetal liver is derived from three sources (1) the hepatic arteries, (2) the umbilical vein, (3) the portal vein The hepatic arteries, arising from the descending aorta are relatively small vessels, and records in which they are seen filled with contrast medium indicate that the amount of blood supplied to the liver from this source is negligible as compared with that derived from the umbilical and portal veins respectively

The Umbilical Venous Inflow

The radiographs reproduced in fig 34 are taken from a record of an injection of contrast medium into one of the two umbilical veins within the cord and show various stages in its passage through the liver The contrast medium enters the liver by a large single vessel the common umbilical vein (produced by the fusion of the two umbilical veins within the cord at a point just proximal to the umbilicus) and is distributed by a number of branches to a considerable area of the liver lying on either side of the vessel This area is often clearly defined in our records (see, e g fig 36) As these branches of the umbilical vein are given off, the calibre of the vein itself progressively diminishes From the termination of the umbilical vein the contrast medium is discharged (1) through the ductus venosus into the posterior vena cava, and (2) into the so-called 'portal sinus' and its small offshoots In the later parts of the record, the contrast medium which has passed to the liver substance is seen collecting in the hepatic veins which drain this area and passing into the posterior vena cava

It will thus be seen that the blood returning to the foetus via the umbilical vein passes to the posterior vena cava (and thence to the heart) by two routes



FIG 33—Goat foetus (136/147 days) Frame from a record of a posterior caval injection made 44 minutes after delivery and 37 minutes after removal of the nose bag and division of the cord The contrast medium passes in its entirety through the right heart to the pulmonary trunk and pulmonary arteries thus indicating that both the foramen ovale and the ductus arteriosus are functionally closed Note the constriction of the posterior vena cava at the level of the diaphragm suggesting the presence of a caval band (see footnote on p 57)

(1) *directly*, via the ductus venosus, and (2) *indirectly*, after passage through the liver tissue, by certain hepatic veins

The ductus venosus is a foetal channel which does not persist up to full-term in all animals, but in the sheep foetus it increases in size and functions as a short circuit for the re-oxygenated blood returning from the placenta right up to birth The early post-natal functional closure of this vessel, as indicated by certain of our radiographic records, is discussed in some detail in Chapter VI

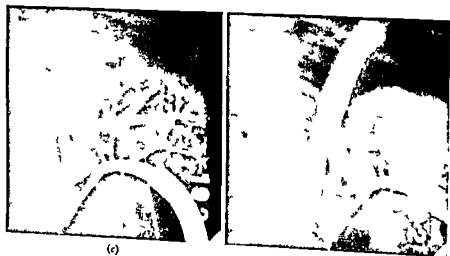
The "portal sinus"—With one or two exceptions (e g fig 36), contrast medium injected into one of the umbilical veins within the cord has invariably passed to the far end of the "portal sinus" It may be objected that this observation does not necessarily represent the normal flow, since the umbilical venous pressure may have been unduly raised by such injections Evidence that the sinus is normally supplied from the umbilical vein is, however, available from experiments in which contrast medium injected into the jugular vein, and allowed time to circulate through the placenta, has been seen on returning along the umbilical vein to pass down the "portal sinus", in such experiments there can have been no question of an unduly raised umbilical venous pressure Further, as will be seen in the example quoted below, there is no indication in our records that blood entering the liver from the portal vein passes up the sinus so long as the placental circulation continues in full vigour

The Portal Venous Inflow

The venous drainage of many of the abdominal viscera is finally collected in the portal vein, a vessel of considerable size, but not nearly as large as the umbilical vein To demonstrate the distribution of the blood entering the foetal liver by the portal vein, injections of contrast medium were made into one of the larger mesenteric veins while the placental circulation was continuing through the intact umbilical cord In fig 35 are reproduced three frames selected from a record of such an injection The contrast medium passes up the portal vein, and on entering the liver is distributed by numerous branches



(a) (b)



(c) (d)

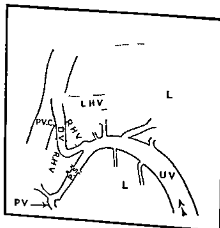


FIG 34 —Sheep foetus (126/147 days) Nose bag on Cord undivided Selected frames from a record of an umbilical vein injection showing various stages in its passage through the liver Note the progressive diminution in the calibre of the umbilical vein *U V* as it gives off its branches to the liver *L* and the passage of the contrast medium through the ductus venosus *D V* to the posterior vena cava *P V C* Note also that the contrast medium passes from the umbilical vein to the far end of the portal sinus (sinus intermedius) *P S* *L H V* *R H V* left and right hepatic veins *P V* portal vein

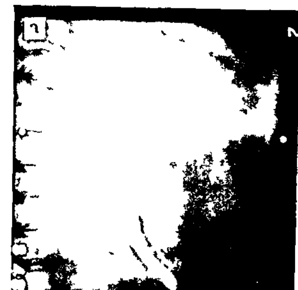




Fig 35

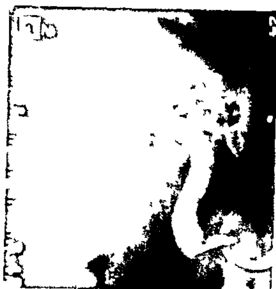




Fig 36



FIG 37

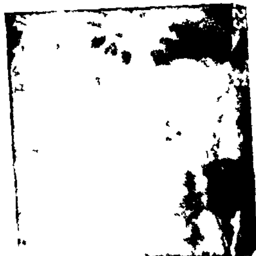


FIG 38

FIG 37—Same animal as that shown in figs 35 and 36 Frame from a record of a mesenteric vein injection made 5 minutes after division of the cord showing the distribution of the portal venous blood after cessation of the placental flow In addition to supplying the area of the liver shown in fig 35 the portal vein has taken over the supply of the area previously supplied by the umbilical vein (fig 36) Note the diminished calibre of the umbilical vein (cf fig 36a) The ductus venosus is still patent but the fainter shadow of this vessel indicates that the flow through it is considerably less than before

FIG 38—Same animal again Another mesenteric vein injection made 20 minutes later (i e 25 minutes from division of the cord) shows no contrast medium passing through the ductus venosus which is functionally closed

to a well defined area of the viscus No part of it is seen to pass up the portal sinus which presumably, is being filled with non opaque blood from the umbilical vein In due course the contrast medium passes through the liver tissue and is carried to the posterior vena cava by those hepatic veins concerned with the drainage of this portion of the liver (fig 35c)

The radiographs reproduced in fig 36 are taken from a record of an umbilical vein injection made a few minutes after that seen in fig 35 and show in the same animal the area of the liver supplied from the umbilical vein In this case—an exceptional one in which the umbilical venous pressure was presumably unduly low—the contrast medium does not pass from the umbilical vein into the "portal sinus" and its offshoots, and hence the area of supply is not quite completely shown

Detailed accounts of the anatomy of the liver of the sheep foetus and of the relative distributions of the afferent and efferent venous systems, as first indicated by our radiographic studies, are given in Chapters III and IV

The Distribution of the Portal Venous Inflow after Cessation of the Placental Circulation

When the placental circulation ceases on division of the umbilical cord after birth the blood from the portal vein is distributed not only to the circum-

FIG 35—Sheep foetus (140 147 days) Nose bag on *Cord undivided* Selected frames from a record of a mesenteric vein injection showing the area of the liver supplied by the portal vein so long as the placental flow continues in full vigour

FIG 36—Same animal as that shown in fig 35 but *4 minutes later* Selected frames from a record of an umbilical vein injection showing the area of the liver supplied from this source (cf fig 35) In this instance (an exceptional one) the contrast medium did not pass down the "portal sinus" and into its offshoots hence the area here shown is not quite the complete umbilical supply area

Fig 35

Fig 36

PART THREE

THE FULL STORY IN A PARTICULAR SPECIES (THE SHEEP, *OVIS ARIES*)

CHAPTER III

The Cardiovascular System in the Mature Foetal Lamb

THIS Chapter deals with those parts of the cardiovascular system which have a bearing on the succeeding physiological story (Chapters IV to VI) The order of the present chapter corresponds, so far as possible, with that of Chapter IV

The lie of the various organs in relation to the three planes of the body, is defined by the use of the opposing terms *cranial* and *caudal*, *sternal* or *ventral* and *dorsal* and *right* and *left* In a number of instances, foetal structures have been given new names, for of the terms in current use

(1) some are per se inappropriate

(2) others have the sanction of embryology but are not really applicable to the mature foetus or at all events not if one interprets structure in terms of function,

(3) others have been borrowed from post natal anatomy and are unsuited to the foetal structures from which that post-natal anatomy has, after considerable changes been evolved,

(4) others again give no suggestion of the known functions of the parts,

(5) others finally help to preserve an incorrect outlook bequeathed from the past

The changes that have been made are not so numerous as the above list of reasons would lead one to anticipate and the new terms are already in use in a number of places So one is encouraged to hope that they may gain more general and perhaps even universal acceptance

It is the view of the present writers that the alterations in the pattern of the cardiovascular system from its first appearance onwards should be regarded primarily as functional adaptations to the ever varying needs of the developing organism and should not be considered, from a physiological point of view, merely as steps in the evolution of the adult system At all times the cardiovascular apparatus is to be regarded as functionally appropriate to the organism under the conditions obtaining at the moment, even if certain mechanisms that will effect the next changes are simultaneously being elaborated (e g in the ductus arteriosus in the latter part of gestation) This outlook would make it difficult to give the full story of the circulation during the earlier stages of intrauterine life for the changes at that time are both numerous and rapid Fortunately however it is only the terminal stage with which this book is concerned, and during that closing period of intra uterine existence the picture undergoes no serious alteration The sudden and dramatic metamorphosis that occurs

scribed area of the liver seen in fig 35, but also to those parts of the viscus which in the foetal stage are supplied with blood returning from the placenta by the umbilical vein Fig 37 is taken from a record of a mesenteric vein injection in the same animal as that shown in figs 35 and 36, made 5 minutes after division of the umbilical cord (the nose-bag had been removed 21 minutes previously) The early distribution of the contrast medium on entering the liver by the portal vein is similar to that seen in fig 35, but in addition the opaque stream is seen passing up the portal sinus into the umbilical vein (now much reduced in calibre, cf fig 36*a*) and its branches The ductus venosus is still patent, although the shadow in this vessel is considerably less than that seen in fig 36*a* In fig 38, taken from a record of a similar injection 20 minutes later, no shadow is seen in the ductus venosus, and this vessel may therefore be considered to be functionally closed

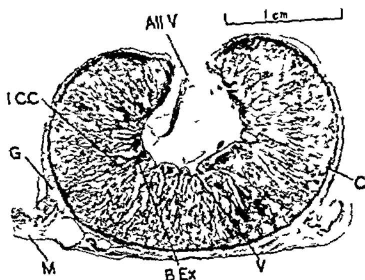


FIG 39—Sheep Section through the placentome (cotyledon and caruncle) at the 100th day of pregnancy *All V* foetal blood vessels in the allanto-chorionic mesenchyme *V* base of one of the arborescent secondary laminae or villi which radiate from the central villus *B.Ex* blood extravasation between the bases of the villi resulting from the rupture of blood vessels which traverse the surface of the intercrypt columns *I C C* *C* fundus of crypt in uterine mucosa *G* uterine glands *M* muscular wall of the uterus

chorial (fig 104) i e the placental membrane, or layer separating the maternal blood from the foetal blood comprises maternal endothelium and connective tissue uterine lumen, and foetal trophoblast (chorion) connective tissue and endothelium

(ii) THE UMBILICAL CORD, THE UMBILICAL VENAE COMITES AND THE SINGLE UMBILICAL VEIN RESULTING FROM THEIR FUSION

The umbilical cord of the lamb (fig 40) contains two arteries and two veins many small blood vessels the allantoic duct and a semi fluid Wharton's jelly The length of the cord is not easily determined because of its retractive power, but it is often of the order of 20 to 25 cm and it does not show the extreme individual variations that the human cord does

No detailed description of the cord will be given here but certain points will be stressed The large blood vessels are commonly, though not invariably, tortuous, and they appear to retain fairly uniform calibres throughout their course in the normal, functioning cord, with the lumina of the veins tending to exceed somewhat those of the arteries If one looks at the vessels through the outer layers of the living cord it is not too easy to distinguish the arteries from the veins unless one is able to see the pulsation in the former The semi fluid character of the Wharton's jelly allows the proximal portion of a divided artery or vein to retract towards the umbilical ring the attachments of the veins to the internal part of the ring prevent any further immediate retraction, but the

during, and shortly after, birth is therefore the sole important change that needs to be described, and an account of it is given in Chapters V and VI below

In the present Chapter the various parts of the cardiovascular system of the mature foetal lamb will be considered in the following order

(i) The placenta
(ii) The umbilical cord, the umbilical venae comites and the single umbilical vein resulting from their fusion
(iii) The liver and its vessels
(iv) The ductus venosus
(v) The posterior caval channel and its terminal bifurcation
(vi) The heart in general
(vii) The lungs
(viii) The pulmonary veins and the relations of their openings to the via sinistra
(ix) The left atrium
(x) The left ventricle
(xi) The ascending aorta and its branches, namely, the coronary and brachiocephalic arteries
(xii) The anterior caval channel
(xiii) The crista interveniens (intervenous tubercle)
(xiv) The azygos venous system
(xv) The coronary sinus
(xvi) The right atrium
(xvii) The right ventricle
(xviii) The pulmonary trunk
(xix) The pulmonary arteries
(xx) The ductus arteriosus
(xxi) The descending aorta and its terminal branches, namely, the umbilical arteries

(i) THE PLACENTA

The structure commonly referred to as the placenta is, properly speaking, the chorio-allantoic placenta, and the classification of such placentae in the eutherian mammals is dealt with at some length in Chapter VII, section (i), readers unacquainted with the system should read through that section before beginning on the present one

The gross shape of the ovine placenta is cotyledonary or multiplex, i e it is divided into a large number of separate, scattered small masses called cotyledons,[1] each with its own arterial and venous supply A cotyledonary placenta (bovine) is depicted in fig 100a, a section through a single ovine placentome, i e through a cotyledon and the uterine caruncle with which it is in contact, is depicted in fig 39 The villi are long and much-branched, and the class to which the placenta belongs, on the basis of its finer structure, is the syndesmo-

[1] The terms for the foetal masses and for the portions of the uterine wall with which they are in contact are numerous and they are not completely appropriate to all cotyledonary types at all stages In addition some terms are used in different senses by different authors

looser connections of the arteries at the same point allow them to continue their retraction and to become intra-abdominal The converse is also held to be true namely, that traction on the cord can pull out of the abdomen the distal ends of the intra abdominal portions of the arteries These arrangements were noted by Meyer (1914, a, b) and were regarded by him as typical of ruminants They are of importance during, and shortly after, birth

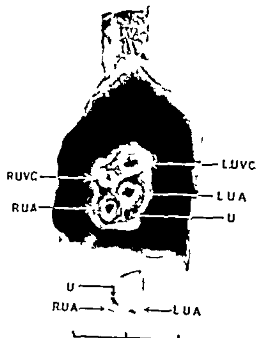


FIG 41 —Sheep foetus nearly full term Umbilical region with cord cut off flush with skin *RUVC LUVC* right and left umbilical venae comites *RUA LUA* right and left umbilical arteries *UV* umbilical vein *U* urachus Scale in cm

The presence of smaller blood vessels within the intact cord was perhaps first noted so far as the lamb is concerned, by Morel and Gernez (1939) but Jordan (1919) had previously reported similar findings in the pig and Meyer (1914 b) had mentioned small vessels in the umbilical stump of the newborn lamb Morel and Gernez considered that the vessels seen by them were probably vasa vasorum Harper (1943), who has independently rediscovered them, says (personal communication) that "many act as vasa vasorum to the main umbilical vessels but the majority are clearly nutritive to the allantoic duct (a very long structure in the sheep) the general connective tissue and ectodermal covering of the cord" Similar vessels are absent from the cords of Man and some of the other mammals so far investigated, research is still in progress in respect of their function in the lamb s cord

The umbilical ring (fig 41) can be regarded as divided into two parts The more cranial of these is occupied by the veins, the more caudal by the arteries and allantoic duct One artery and one vein lie to the right and one artery and one vein to the left of the mid line of the body The duct lies centrally, just caudal to the arteries The arterial section of the ring can contract down after the severed arteries have retracted into the abdomen, the same is apparently true of the venous section after the delayed post partum liberation of the veins (Meyer, 1914 a b)

A good diagram of the cord and its contained structures does not seem to be available Morel and Gernez, in their fig 1 gave a picture of part of the cord, but the calibres of the vessels are not in agreement with radiographic findings in the living subject

So much for the cord as a whole, one may now pass to the two veins These fuse within the foetus to form a single channel and it is awkward to have to use the same term "umbilical vein," for three different vessels In

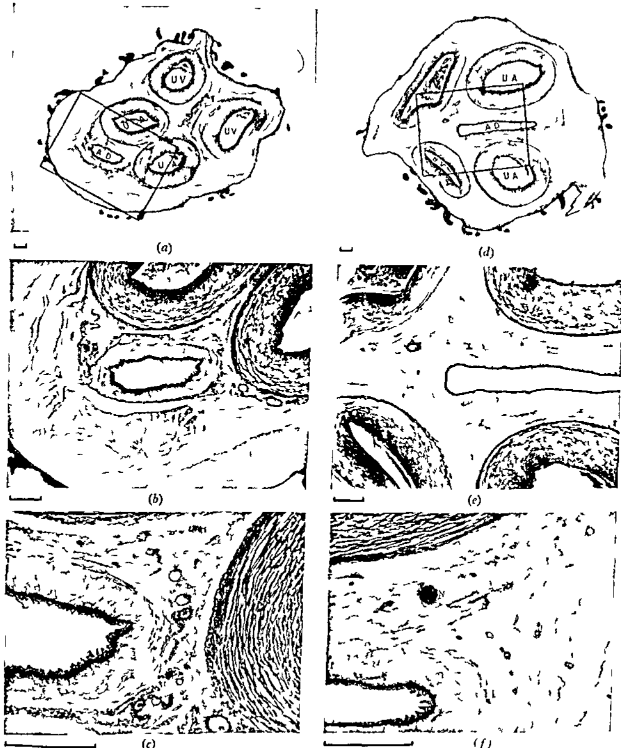


FIG 40 —Sheep foetus c 100/147 days Transverse sections of umbilical cord *U A* umbilical artery *U V* umbilical vena comes *A D* allantoic duct Scales = approx 0 5 mm *a* low power view of proximal end of cord close to body wall of foetus *b* higher power view of area enclosed by continuous lines in *a* *c* still higher power view of area enclosed by interrupted lines in *a* *d* low power view of distal end of cord close to chorion Allantoic duct commencing to dilate *e* higher power view of area enclosed by continuous lines in *d* *f* still higher power view of area enclosed by interrupted lines in *d* Note that the small vessels present in the cord appear to be concentrated round the allantoic duct Compare figs 108 and 109

picture of the vascular tube as a whole, and this can be produced only by reconstructions from serial sections, duly correlated with evidence from macroscopical dissection and other sources Here and there, in connection with parts of the foetal cardiovascular system, some progress has been made upon these lines but in respect of no single vessel is the full picture available and in respect of most vessels it has not even been begun

Meyer's description was derived from studies of newborn lambs, briefly it ran as follows The most striking feature is the variability in the amount and distribution of the longitudinal musculature of the media, which is present in the venae comites within the cord, but is absent from the intra-abdominal vein In the cord the venae comites have a structure very akin to that of the arteries There is a single layered endothelium, and [? always, or only often] an internal elastic membrane The media contains both longitudinal and circular muscle fibres The former are somewhat irregularly distributed with elastic fibres between them, they are not grouped in bundles among the fibres of the much thicker circularis as is usually the case in the arteries The circular fibres are arranged rather loosely, especially at the periphery They lie in concentric layers, those in the peripheral layers being more definite No true adventitia can be said to exist, though a number of small blood vessels are found in the perivascular tissue Inside the abdomen the venae comites have a similar structure except that the muscle fibres interlace and circular fibres are extremely few in number In the umbilical vein there is no internal elastic membrane and no longitudinal musculature The provision of circular muscle fibres is relatively small and they are more closely apposed There is a fairly definite, vascular adventitia

(iii) THE LIVER AND ITS VESSELS

In earlier sheep foetuses, i e at about half term, the liver is nearly symmetrically placed in relation to the ventro dorsal mid line of the body, the umbilical fissure or fossa is near to that mid line and to the umbilicus and the umbilical venae comites may still be separate vessels right up to the ventral edge of the liver In addition, the organ may contribute over a tenth of the total body weight, as opposed to the thirtieth or less that it contributes at full term (Barclay Franklin and Prichard, 1942, c) In the living mature foetus a small portion only of the liver lies to the left of the dorso ventral mid line, and the umbilical fissure lies well to the right of this mid line and an appreciable distance from the umbilicus

The external appearance is shown in fig 42 There is a fair sized papillary process partially overlapping the portal sinus " and a relatively large caudate process both are partially separated from the rest of the organ A gall-bladder is present The umbilical vein and " portal sinus" lie close to the visceral surface The posterior vena cava is partly or wholly surrounded by liver tissue in the hepatic part of its course

More interesting than the external appearance however, are the internal vascular arrangements An earlier account of these was given by Klages (1931) but he had no experimental findings to guide him, so the following

the rest of this book, therefore, the term "umbilical venae comites" will be used for the twin veins and the term "umbilical vein" will be reserved for the larger vessel resulting from their fusion

Macroscopically, the venae comites are seen to result from the unions of smaller vessels which return blood from the cotyledons, and all these vessels, as well as the umbilical vein itself, are valveless In the radiographic records of the functioning umbilical cord, the internal calibre of the venae comites is seen to be of the order of 4 to 6 mm Their length is about 30 to 40 cm As the average flow through one vena comes is about 200 c c per minute, and the average cross-section about 0 2 sq cm, the rate of the blood flow should be about 16 cm per second, and it should take about 2 to 2 5 seconds for blood to pass right through a vena comes No radiographic records are available to confirm this estimate, but it is in reasonable accord with the total circuit time from umbilicus to cotyledons and back (see Chapter IV), so it is probably not far wrong

Within the cord the venae comites are obviously very muscular and they contract down rapidly and markedly in response to certain kinds of mechanical stimulation, the relatively local character of the contraction suggests that it is a direct muscular effect rather than a reflex one At, or near, the umbilicus the veins appear to be specially contractile (Barclay, Franklin and Prichard, 1942, c) and at this point they usually exhibit some degree of narrowing in radiographic records of the living animal

At or not far from their entry into the foetus, the twin veins fuse externally along their surface of contact They pass through the skin almost perpendicularly to the external surface but, once through it, they bend (sometimes very sharply) cranially, and they also incline about 10–15° to the right from the ventro dorsal mid-line of the body There must be a distinct difference between the extra- and intra-foetal portions of the vessels, for a contraction has never been seen to spread from the former to the latter, and in fixed specimens the former are contracted and thick-walled, the latter wide and thin-walled About 2 cm from the point at which they pass through the skin of the foetus, the vessels fuse internally, the "party-wall" between them terminating in a crescentic edge, concave towards the liver There is, apparently, no differential distribution within the foetus of the blood streams from the two venae comites (Franklin, Barclay and Prichard, 1940, 76)

About 2 cm proximal to the point at which they fuse internally to form the umbilical vein, this single vessel reaches the border of the liver (in fixed specimens about 1 3 cm to the right of the ventro-dorsal mid-line of the body), and thereafter it passes for about another 1 cm within a fossa before actually penetrating into the liver substance itself The remainder of its course is described in the next section

An account of the microscopical structure of the venae comites and of the umbilical vein is necessary for the full appreciation of the post-natal changes, and Meyer (1914, b) gave such an account One must, however, repeat here a complaint already made elsewhere (Franklin, 1937, 35–6), namely, that descriptions of cross-sections and longitudinal sections of vessels are of themselves inadequate What the physiologist requires from the anatomist is a

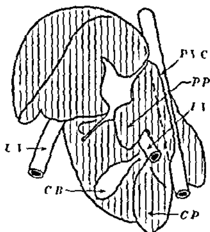


FIG 43—Sheep foetus 139 147 days View of liver from left (the posterior vena cava is straight and of uniform calibre because it was fixed with a glass rod in it) *U V* umbilical vein *P V* portal vein *P V C* posterior vena cava *I P* papillary process *C P* caudate process *G B* gall bladder Scale in cm

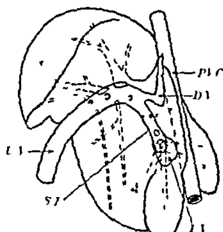


FIG 44—Same liver as in fig 43 with small superficial portions removed and the umbilical vein *U V* portal vein *P V* sinus intermedius (portal sinus) *S I* and ductus venosus *D V* opened up Interrupted lines indicate offshoots from the main veins to the liver tissue *V C* posterior vena cava Scale in cm

—or in some cases two offshoots—passes to the left-most portion of the liver It is convenient as will be shown later in this book, to style these liver masses supplied by the umbilical vein, the central mass (subdivided into central mass right and central mass left) and left mass respectively The final large offshoot that goes to the left mass is what Rex (1888) called, in the post natal liver, the ramus angularis ' No offshoots from the other afferent vein of the liver i e the portal vein supply any part of the central mass or left mass In a fixed specimen the umbilical vein may show no appreciable decrement in calibre in its intra hepatic course (fig 44) In the living foetus, on the other hand, its calibre decreases progressively as branches are given off, and its final width may be little more than a third of its initial one (see fig 34*b*)

The radiographic records of the living foetus also show that the vein is continued functionally by the ductus venosus and by the "portal sinus' The ductus in this genus is a channel that increases in absolute size and continues to act as a short circuit right up to birth (Barclay, Franklin and Prichard 1942, c) It will be considered in detail below so one can pass straight on to the evidence about the sinus The first point is that contrast medium injected into one of the umbilical venae comites in the cord of the living foetus, has almost invariably gone right to the far end of the sinus In case it is objected that the umbilical venous pressure may have been unduly raised by such injections one can add that contrast medium, injected into the external jugular vein and thereafter allowed time for the circuit through the cotyledons has similarly travelled as far as the portal end of the sinus In such experiments, there could have been no undue increase in umbilical venous pressure and the

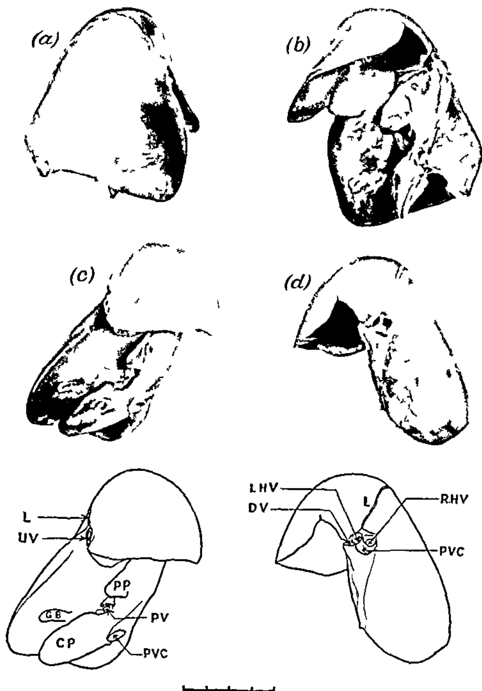


FIG 42—Sheep foetus c 140/147 days Views of liver from (a) right (b) left (c) ventral and (d) dorsal aspects together with keys to (c) and (d) *U V* umbilical vein *L* ligament *P P* papillary process *C P* caudate process *G B* gall bladder *P V* portal vein *L H V* left hepatic vein *R H V* right hepatic vein *D V* ductus venosus *P V C* posterior vena cava Scale in cm

description supersedes his The umbilical vein (figs 43, 44) enters the liver tissue about 1 cm from the ventral border of the organ and several offshoots leave it between that point and its generally accepted anatomical termination, i e the beginning of the "portal sinus" The first offshoots are distributed to the portions of liver lying on either side of the vein, the final large offshoot

it is possible to state that the amount of blood entering the liver through its arteries must be insignificant beside that entering through the umbilical and portal veins

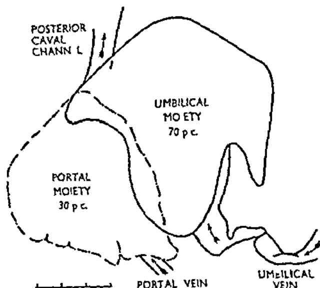


Fig 45 —Sheep foetus 140 147 days Outline drawing of liver from the right aspect to show division of the viscus (as radiographicall determined during life) into umbilical and portal moieties Scale in cm

The efferent vessels of the liver are the accessory hepatic veins that open into the posterior vena cava and the large right and left hepatic veins and the ductus venosus, which unite with the posterior vena cava about the level of the diaphragm (fig 42*d*) Klages (1931) described the individual vessels in some detail but the following account is entirely independent of his and was written with a different object The accessory veins, variable both in number and in size, collect almost exclusively blood that has been distributed to the liver through offshoots of the portal vein The right hepatic vein, which corresponds to the right and middle hepatic veins of many genera, is often formed by the union of two minor trunks one of which collects mainly from the portal moiety of the liver (in so far as this is not drained by accessory veins) and the other mainly from central mass right (fig 46) The left hand limit of this mass on the diaphragmatic surface of the liver is an imaginary straight line drawn between the middle of the entering umbilical vein and the right hand edge of the termination of the left hepatic vein The ' catchment area ' of the right hepatic vein always seems to end at this line, but there is often some overlapping of the ' catchment areas " of its subsidiary trunks The left hepatic vein collects from central mass left and the left mass i e from the greater part of the umbilical moiety of the liver (fig 46) On the whole, the efferent veins of the liver tend to lie more cranially

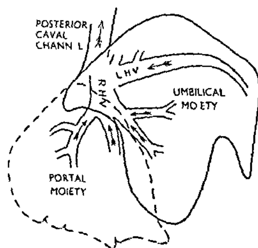


Fig 46 —Same liver as in fig 45 to show hepatic venous drainage *RHV* *LHV* right and left hepatic veins Scale in cm

cord was intact As this defence is adequate of itself, there is no need to adduce the further ones that are available It is clear, then, that umbilical blood goes the whole length of the sinus The counterpart to this finding, i e the evidence that no portal blood passes into the sinus, is provided by records of experiments in which contrast medium was injected into the main mesenteric vein, for none passed from the portal system into the sinus, despite the fact that the amount injected in unit time probably exceeded the normal flow through the mesenteric vein It is clear from the above evidence that, so far as the mature foetal lamb is concerned, the epithet "portal" applied to the sinus is physiologically a misnomer and that there is justification for substituting the epithet "umbilical" But, until comparative radiographic or other studies have shown that the findings in the foetal lamb are probably of universal application, it is more convenient to adopt a less functional epithet, and the one that will be used in the rest of this account is "*intermedius*," in as much as the sinus lies between the anatomical terminations of the umbilical and portal veins The term used by Klages was "pons intervenosus" or "Brucke" The sinus may send a few very small offshoots to other neighbouring parts, but these are insignificant by comparison with those that pass to the papillary process As this is the final intra-hepatic distribution of the umbilical venous inflow, one is able to say that the umbilical moiety of the liver, i e that part which gets its afferent venous supply from the umbilical vein, is composed of the right and left parts of the central mass, the left mass, and the papillary process

The rest of the liver, i e what it is convenient to refer to as the right mass, together with the caudate process, gets its afferent venous supply from the portal venous inflow and can be styled the portal moiety of the organ The functioning portal vein is nowhere near so wide a vessel as the functioning umbilical vein, in figs 35 and 36, for instance, which are taken from the records of a 140-days' lamb, the calibres are as 3 to 5, i e the cross-sections of the vessels are as 9 to 25 or, roughly, 1 to 3 At its termination, which is not far inside the liver tissue, the portal vein sends a number of fair-sized offshoots to the right mass and the caudate process (figs 44, 35*a*)

In each of two mature foetuses specially studied, the umbilical and portal moieties were clearly demarcated as a result of injections made into an umbilical vena comes and into the main mesenteric vein respectively Fig 36*a* is a frame from the record of the first foetus, it shows the umbilical injection before the demarcation of the umbilical moiety had been completed Fig 35*a* is a frame from the record of the corresponding mesenteric injection, it shows the portal moiety nearly fully demarcated From the double records of this foetus it was possible to construct fig 45, which served as a guide for the post mortem division of the fixed liver into its two moieties The two parts were weighed and were found to contribute 70 and 30 per cent respectively of the total liver weight The correctness of the division was proved by subsequent probing of the umbilical and portal offshoots In the second foetus, the percentages were very similar, namely, 67 and 33

So far, the afferent arterial supply of the liver has not been mentioned In a number of instances the calibres of the functioning hepatic arteries have been demonstrated by the entry of contrast medium into these vessels As a result,

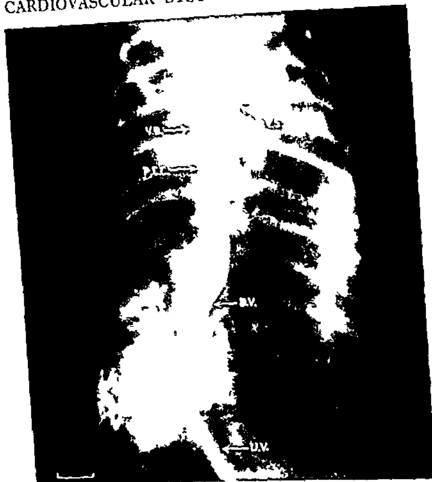


FIG 47.—Sheep foetus 140/147 days. Frame from a direct cineradiographic record of an umbilical vein injection. The foetus is lying supine. *U.V.* umbilical vein; *D.V.* ductus venosus; *P.C.C.* posterior caval channel bifurcating above apparently into its terminal left *V.S.* and right *V.D.* divisions. Scale = cm on radiographic record.

at the site of the "lipping." As the Nuffield Institute team included no histologist, the further investigations were put in the hands of Barron and of Amoroso who independently found adequate microscopical evidence of the presence of a "sphincter" exactly where the macroscopic and radiographic studies had indicated that one should exist. In consequence the physiological story was released for publication (Barclay, Franklin and Prichard, 1942 a); it is to be found in the later chapters of this book.

A photograph of the sphincter occluding part of the opening from the umbilical vein into the ductus is reproduced as fig. 48*a*: the appearance is somewhat reminiscent of that of the iris of the eye, but the analogy should not be pressed, for there are no radial smooth muscle fibres in the sphincter and there is at present no clear cut evidence about its innervation. The degree of contraction exhibited by it varies according to circumstances. Histologically

than the corresponding afferent veins The main hepatic veins, at their terminations, are nearly as wide as the posterior vena cava with which they unite

Before passing on to the next section, one may note that the radio opaque medium, thorotrast, after injection into the circulating blood of the foetal lamb, is not removed from it and concentrated in the liver and spleen This is in marked contrast to its fate in some other animals, e g post-natal kittens and adult cats and dogs (Barclay, Franklin and Prichard, 1942, c), and it would be of interest to discover the reason for the difference

(iv) THE DUCTUS VENOSUS[1]

Klages (1931) gave an earlier account of this channel He examined twelve lambs that died one or more days after birth and found that one of them showed no trace of a ductus , such a finding must, one imagines, be a rare one in this genus Klages described the channel in a 24-hours' lamb as follows It arises as a vessel of 6–7 mm in calibre from the junction of the umbilical vein and the " pons intervenosus " [sinus intermedius] For 10–12 mm it continues in the line of the umbilical vein, then bends at a right angle and, finally, increased to 8 mm in calibre, it enters the posterior vena cava on its visceral side in the middle of the dorsal border of the liver It distributes no offshoots

As a result of their radiographic and anatomical studies, the present writers are in a position to say much more than Klages could In the lamb the ductus appears to increase in absolute size, and to function as a short-circuit between the umbilical vein and the posterior caval channel, right up to birth When contrast medium is injected into one of the umbilical venae comites, that part of it which goes through the ductus readily outdistances the remainder which makes the hepatic circuit This is seen not only in the lateral radiographs (e g in fig 36*a*), but also in the few ventro-dorsal ones that have been obtained (see, e g , fig 47) This last figure also suggests that the functioning ductus is not appreciably narrower from right to left than it is ventro-dorsally , this is of importance if one is to visualize the channel in a three-dimensional aspect In the seasons 1938–9, when co-operating with Barcroft and Barron, the present writers made no very serious examination of the anatomy of the foetal lamb Before the next season, preliminary historical studies had not only provided a number of physiological questions to be answered, but had also shown, very clearly, that anatomical investigations must be carried out pari passu with the more functional ones It was some rather faint recollection of Bichat's statement about the ductus that led to a more detailed examination of its beginning in a series of fixed specimens , a passing reference was made almost at once (Franklin, Barclay and Prichard, 1940) to the findings, but a proper account of them was deferred, for as yet the function of the " lipping ' at the beginning of the ductus was not known Shortly afterwards, however, a more thoroughgoing examination of the radiographic records secured in the 1940 season showed that there was reason to suspect a ' sphincter mechanism "

[1] In addition to the figs referred to in the text see Plate V and figs 80 81 83 84

are all obvious in the various radiographs that have been reproduced (see, e g , figs 34 36) so there is no need for further comment on these features The channel ends to the left of the opening of the left hepatic vein, and ventral to the posterior vena cava (fig 42*d*)

(v) THE POSTERIOR CAVAL CHANNEL AND ITS TERMINAL BIFURCATION

There are three main reasons for introducing the term "posterior caval channel' The first of these is that, in the mature foetus, the meeting of the main hepatic veins the ductus venosus, and the posterior vena cava is to be regarded as a union of vessels rather than as an entry of subsidiary vessels (the hepatic veins and the ductus) into a main trunk (the posterior vena cava) It is logically necessary therefore, to find some term other than "posterior vena cava' for the vessel formed by the union The second reason is that this vessel is functionally more important as a continuation of the umbilical vein than as a continuation of the posterior vena cava The third reason is that the channel terminates within the heart beyond the accepted anatomical limits of the posterior vena cava

With regard to the first of these points one can say that in the living foetus the posterior vena cava tends to be wider than any of the other three vessels, but that often there is not much difference in calibre between it and say, the left hepatic vein This concept of the vena cava as merely prima inter pares is strengthened if one examines a fresh specimen The vena cava is seen on the dorsal aspect and ventral to it from left to right, are the ductus venosus and left and right hepatic veins The four channels are separated only by thin membranous septa that must yield freely to permit variations in the individual blood flows The free borders of the septa are at approximately the same level though this is subject to individual variations Incidentally the directions of the long axes of the four vessels are such that blood moving caudally in the posterior caval channel goes more readily into the vena cava the ductus and the left hepatic vein than it does into the right hepatic vein (Barclay, Franklin and Prichard 1942 c)

With regard to the second point, the most important part of the blood that flows through the posterior caval channel is obviously that coming directly (via the ductus venosus) and indirectly (via the hepatic veins) from the cotyledons for it is this blood that carries fresh supplies of oxygen for distribution to, and by the heart So functionally the channel has its major significance as the termination of the pathway from the cotyledons to the heart It is not possible at present to say at all precisely what percentzges of the total flow through the channel are contributed by umbilical blood and by blood from other sources respectively but it appears probable that the umbilical flow contributes the major portion (see Chapter IV)

With regard to the third point, the combined ductus venosus, hepatic and posterior caval flow cannot be described as having reached the atria when it has reached the accepted anatomical termination of the posterior vena cava For one can remove this vessel completely (fig 49) and still see within the heart the prominent ridge on which the flow divides into left and right terminal streams

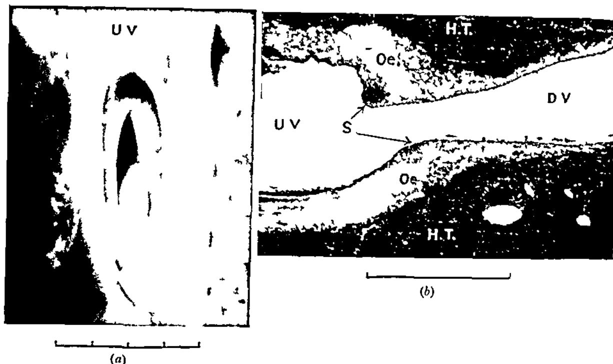


FIG 48—*a* Sheep foetus nearly full term Somewhat oblique view of umbilical vein *U V* opened up to expose *iris like sphincter (centre of fig) at beginning of ductus venosus* Scale in mm *b* Sheep foetus nearly full term Longitudinal section (top of fig cranial bottom caudal) across junction of umbilical vein *U V* and ductus venosus *D V* to show smooth muscle sphincter *S* at beginning of latter Note more pronounced concentration of circular muscle fibres of sphincter on cranial aspect and widening of ductus venosus immediately proximal to sphincter *Oe* oedema (see text) *H T* hepatic tissue Scale 1 mm

(fig 48*b*), it is seen to be a relatively strong, localized collection of circular smooth muscle fibres, *separated by an oedematous layer from the hepatic tissue* proper, the vascularity of the surroundings is noticeable According to Barron (1944, 278), the nerve supply is via fibres which course with the two vagi but thereafter unite to form a separate nerve These fibres have endings of motor type in the musculature, and the absence of demonstrable ganglion cells suggests that they constitute a post-ganglionic sympathetic, and not a pre-ganglionic parasympathetic, innervation This suggestion is in line with the results of vagal stimulation in the neck region of the living foetus, for radiographic records made during such stimulation failed to show any contraction of the sphincter (Barclay, Franklin and Prichard, 1942, c) On the other hand, further work is probably required before one can accept such negative findings as final In Amoroso's view, the oedema round the sphincter is very possibly concerned in the functional closure of the ductus, but at the moment he is not prepared to say more than this

At its origin, with the sphincter uncontracted, the functioning ductus venosus has a calibre about one-third of that of the umbilical vein at its entry into the liver *If one assumes, as seems justified by a comparison of lateral and* ventro-dorsal radiographs, that both channels are more or less circular in section, then the cross-section of the ductus at its beginning is about one-ninth that of the umbilical vein at its entry The course of the by-pass, its marked bend, and its tendency to increase in calibre as it passes towards the vena cava,

Key to Fig. 50

Fig. 50

Fig. 51

Fig. 52

Fig. 53

Key to Fig. 53

Figs. 50–53.—Sheep foetus nearly full term. Successive stages in dissection (see text) of dorsal aspect of heart and great vessels. To show the last part of the posterior caval channel, *ICC*, its intra-cardiac bifurcation and its left and right terminal divisions. *ACC*, anterior caval channel; *RA*, *RV*, right atrium and ventricle; *RAVV*, right atrio-ventricular valve; *ALA*, auricle of left atrium; *LA*, *LV*, left atrium and ventricle; *PTr*, pulmonary trunk; *RPA*, *LPA*, right and left pulmonary arteries; *DA*, ductus arteriosus; *PVR1*, *R2*, *R3* and *4*, *L3*, *L2*, *L1*, pulmonary veins draining respectively the right apical, cardiac, diaphragmatic and intermediate lobes and the left diaphragmatic, cardiac and apical lobes; *A*, aorta; *BCA*, brachiocephalic artery; *AP*, the free or apposable portion (pars libera) of the via sinistra or left terminal division of the posterior caval channel. The via dextra or right terminal division is indicated by the right arrow in the key to fig. 53. Scale in cm.

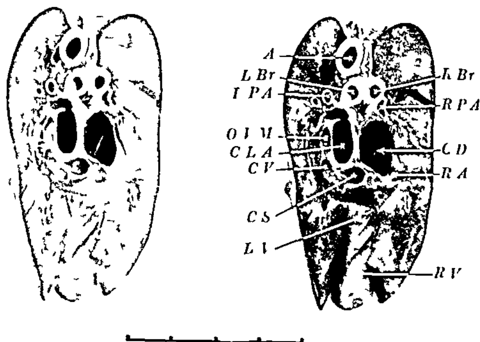


Fig 49 —Lamb 2 days post partum View looking cranially of heart and lungs transected to show dividing ridge or crista dividens C D of posterior caval channel the posterior vena cava itself has been entirely removed *R A* right atrium *C L A* cavity of left atrium *C S* coronary sinus *C V* coronary vein *O V M* oblique vein of Marshall (main azygos drainage route in this genus) *R V* *L V* right and left ventricles *R P A* *L P A* right and left pulmonary arteries *A* aorta *R Br* *L Br* right and left main bronchi Scale in cm

Developmentally, the right and left terminal channels have not the same origin as the vena cava, so one should not speak, as Kilian, for instance, did, of this vein dividing within the heart The posterior caval channel, on the other hand, can be defined so as to include functionally similar, if developmentally different, structures

Figs 50–53 show successive stages in a dissection specially made to demonstrate the last portion of the channel, its intra-cardiac bifurcation, and its two terminal divisions The specimen was a nearly full-term foetus Fig 50 shows the dorsal aspect of the heart and great vessels, even from the outside one receives a suggestion of the division of the channel In fig 51 the right group of pulmonary veins (see section viii below) and part of the left atrial wall are retracted to expose the left terminal division of the channel (in current terminology the foramen ovale and its valve) In fig 52 this tubular passage, with its "cords" or "guy-ropes," is better seen, for the whole of the dorsal wall of the atrium has now been removed, the tube in this specimen is not fully dilated Before fig 53 was made, the dorsal walls of both anterior and posterior caval channels were removed, and the beginning of the right terminal division of the latter is apparent Finally, fig 54 is a photograph taken, without further dissection, from a more caudal aspect One can see the ridge at which the channel bifurcates, the opening (*) of the coronary sinus, and the tree-like appearance of the wall of the auricle of the right atrium There is no Eustachian or Thebesian valve

The term "posterior caval channel" can be latinized as "canalis posterior"

"cords" or "guy-ropes" pass to the atrial wall (figs 52–54) Each such cord, according to Leach (in Franklin, Barclay, and Prichard 1940) consists of a few cardiac muscle fibres encased in a wider layer of collagen fibres The former are not identifiable as Purkinje fibres which is not surprising as such fibres develop well only in the adult

As the collagen fibres would presumably prevent the contraction of the few small muscle fibres, the latter could be looked upon as 'conductile' In the mature foetus there is a fair amount of muscle in the apposable portion of the via sinistra Both this fact and also the presence of the 'cords' have been mentioned at intervals from the seventeenth century onwards, Mosca (1914) was perhaps the last to do so before 1940 There are a few *more* points to be noted about the via sinistra The first is that the entry into it may be circular or elliptical in contour The second is that there *is* a marked diminution in the calibre of the tube between its beginning and its termination The findings in a particular foetus, in which the via was fixed in the fully open position (fig 55) can serve as an example The long and short diameters of the elliptical entry were 10 and 7 *mm* respectively, the total



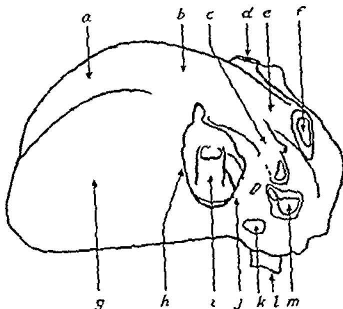


FIG 55—Sheep foetus *c* 140 147 days Photograph taken from the left side of the heart with the auricle *of the left* atrium removed to expose the fully open tubular via sinistra (foramen *ovale*) Unfortunately the guy *ropes* running from the free edge of the tube to the atrial wall had been removed for section before this *photograph* was taken *a* right *ventricle* *b* pulmonary trunk *c* left pulmonary artery *d* brachiocephalic artery *e* ductus *arteriosus* *f* descending aorta *g* left ventricle *h* line of exsection of auricle of left atrium *i* tubular via sinistra *j* edge of circular recess in which lie the via sinistra and the entries *of the* pulmonary veins draining the right apical and cardiac lobes *k* one of the veins from the *left lung* *l* posterior caval channel *m* left main bronchus Scale in cm



FIG 54.—Same as fig 53 but viewed from a somewhat more caudal aspect To show the dividing ridge or crista dividens on which the posterior caval stream divides * Opening of coronary sinus Scale in cm

The prominent ridge has been styled, in accordance with its radiographically determined function, "crista dividens" or "the dividing ridge" The left and right terminal divisions of the canalis posterior require shorter names for general use, and in the rest of this book they will be called "via sinistra" and "via dextra" respectively With the nomenclature to this extent settled, one can proceed to definitions and descriptions The posterior caval channel begins at the union of the ductus venosus the main hepatic veins, and the posterior vena cava Over the greater part of its length, it lies in the furrow provided by the intermediate lobe of the right lung Within the heart it bifurcates, at the dividing ridge, into a via sinistra, leading into the left atrium, and a via dextra, leading into the right atrium The dividing ridge is the curved, free, caudal edge of the inter-atrial septum, unsatisfactorily styled in the past "isthmus of Vieussens," "annulus fossae ovalis," and the like Its appearance and lie are adequately shown in figs 49 and 54 The via sinistra is composed of a "pars firma" or "fixed portion," which is part of the interatrial septum, and a "pars libera" or "free" or "apposable portion" (the so-called "valve of the foramen ovale") The term "foramen ovale" is not a good one, because

(1) it has had, and still does have, too many connotations (Patten, 1931),
(2) the epithet "ovale" is not always correct,
(3) it gives no indication of function, and
(4) it focusses attention on one terminal division only of the posterior caval channel, *and so perpetuates the asymmetry of the past outlook* on the posterior caval inflow

The term "valve of the foramen ovale" is not a good one, because
(1) it is linked with the preceding one, and
(2) in the lamb and in many other animals, the structure in question does not have a valvular appearance

The posterior caval channel inclines slightly to the left as it passes cranially, the via sinistra inclines more to the left and also somewhat sternally, but its main direction, too, is cranial The via dextra, on the other hand, begins by diverging somewhat to the right and ends by bending sharply towards the sternum Hence the via sinistra is more in line than the via dextra with the posterior caval channel, and this disposition of itself favours the passage into the left atrium of the bulk of the posterior caval flow The via sinistra is perhaps, visible in fig 47, both viae, apparently, are visible in fig 30 Just before the via sinistra opens into the left atrium, its apposable portion often shows fenestrations, and from the free border of this portion one or more

about 30° with the mid line, running from about one o'clock cranially to seven o clock caudally From the dorsal aspect the rotation is equally obvious (see, e g fig 52) but now, of course it is counter clockwise i e the plane runs from eleven o'clock to five o clock In consequence of the rotation the right atrium and its auricle and the right ventricle lie more cranially than the corresponding left chambers as one can see in the lateral radiographic records

Whether or not the two ventricles have equally thick walls in the foetus, as Spigel Harvey and others after them claimed is not easy to decide, for the general plans of the two cavities are different, and in consequence it is difficult to know where to make comparable cross sections of their walls On the other hand, there is no doubt that the left ventricle of the adult is much thicker-walled than the right, so parity or slight disparity in the foetus changes to great disparity in the adult

(vii) THE LUNGS (fig 56)

The lungs are not adherent to one another at any point The right lung is appreciably larger than the left lung, the former consists of four lobes, the latter of three On each side if one follows the terminology used by Sisson (1940) there are apical cardiac, and diaphragmatic lobes, on the right side in addition there is an intermediate (or mediastinal or azygos) lobe The right apical lobe overlaps the sternal mid line and there is a corresponding reduction in the more cranial part of the left lung A considerable portion of the right apical lobe lies cranial to the heart, but on the left side it is only the dorsally placed apex of the lobe that does so The lungs cover the heart to an extent that varies with the individual, but the left side of the viscus is invariably more exposed than the right side The lobulation of the lungs is perceptible on the surface but is far less marked than in some foetuses, e g the bovine

The degree of separation of the lobes of the right lung is considerable, but varies somewhat with the individual The apical lobe is commonly subdivided by a partial fissure into cranial and caudal portions sometimes it is subdivided into three portions It is supplied by an apical bronchus Between the sternal borders of the apical and cardiac lobes is the right cardiac notch, sternal to which project parts of the right and left ventricles The intermediate lobe provides a furrow in which lies the major part of the posterior caval channel The lie of the vessel is constant, that of the lobe varies, hence the exact relation of the lobe to the vessel is variable

The lobes of the left lung like those of the right lung show a variable degree of separation, but it is much more marked between the cardiac and diaphragmatic lobes than between the apical and cardiac lobes Indeed it is sometimes difficult to distinguish these two last The left cardiac notch is bigger than the right one and commonly exposes considerable parts of the right and left ventricles and of the auricle of the left atrium, as well as the root (fig 56b *P*) of the pulmonary trunk

The freshly removed lungs appear dark and compact and sections of them sink when placed in water

length of the pars libera between its attached and free borders was 10 mm. The tube decreased in calibre in the first half of its length and had a uniform diameter of 6 mm. from there to its termination. In other foetuses one has seen a more gradual decrease in calibre, in others again an initial decrease followed by a slight increase, and then another decrease. But always the exit has been narrower than the entry. The third point is that the pars libera contributes the major portion of the circumference of the tube; in one case as much as six-sevenths were provided by the pars libera and only one seventh by the pars firma. Normally the disparity is less, but the proportions are always such that the fully open via shows up as a distinct tubular structure on the inner wall of the left atrium. The last point is that the free end of the tube, in the lateral projection, almost overlaps the first portion of the aorta; in the lateral radiographs (see, e.g., fig. 58) the shadow of the left atrium, which extends beyond the end of the tube, may prevent one from getting a clear view of the aortic valve.

There one may leave the via sinistra and pass to the via dextra. In the human foetus, and in all others similarly possessed of a Eustachian valve, the right-hand channel, like the left, is composed of a pars firma and a pars libera (i.e. the valve), and can be regarded as terminating, so far as the latter is concerned, at its free border. In the foetal lamb there is no Eustachian valve, and even a projection that some writers have taken for the rudiment of this valve proves, on probing from the outside, to be nothing but a slight infolding of the wall. So there is no trace of a pars libera viae dextrae in the lamb. The pars firma, on the other hand, can in all foetuses be regarded as ending where the right terminal division of the posterior caval stream meets the anterior caval stream, i.e. at the crista interveniens (tubercle of Lower). This is described in greater detail below, so two further notes will suffice to conclude this account of the via dextra. The first concerns its relation to the opening of the coronary sinus. In a figure referred to earlier (fig. 54), the opening appears to be actually within the via dextra. If, however, one looks at a transverse section through the heart and lungs at the level of the crista interveniens, one can see that the opening of the sinus lies sternal to the medial part of the via and is itself unrelated to the crista. The second point to be made is that the via dextra is a comparatively short channel.

(vi) THE HEART IN GENERAL

In this section a few general points only are noted, for details of the individual chambers and so forth are more appropriately considered later.

As is clearly seen in various lateral radiographs, the heart inclines caudally from base to apex and there is a considerable interval between it and the diaphragm dorsally, though only a very small one sternally. When one looks at the organ from the sternal aspect, one can note the following further points. The apex, which is formed by the left ventricle only, lies either in, or only just to the left of, the sterno-dorsal mid-line of the body. The heart mass as a whole is more or less symmetrically placed on either side of this mid-line, but the plane of separation of the right and left sides of the heart makes an angle of

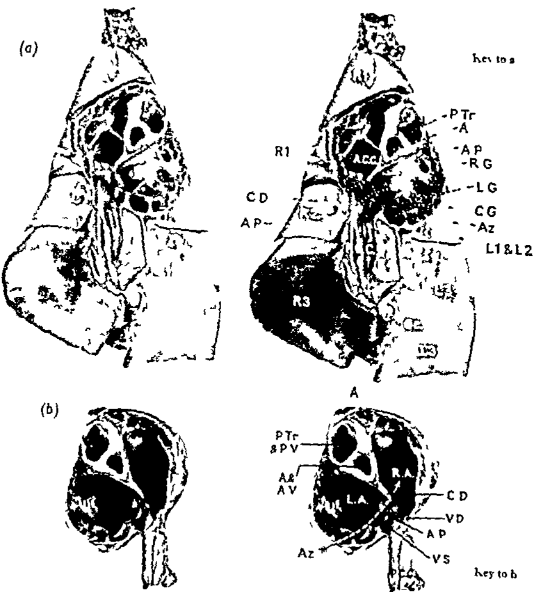
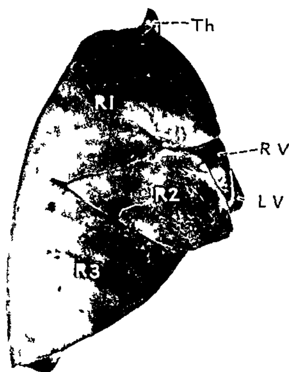
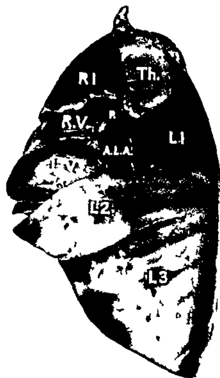


FIG 57.—Sheep foetus c 120–147 days Above photograph of dorsal half of exsected thoracic viscera divided by a side to side cut through the long axis of the posterior caval channel To show the entries of the three groups of pulmonary veins into the left atrium *RG* right group entry dorsal to the free or apposable portion *AP* of the via sinistra which is closed this right group drains the right apical *R 1* and right cardiac *R* lobes *CG* caudal group entry this group drains the right diaphragmatic *R 3* right intermediate *R 4* and left diaphragmatic *L 3* lobes *LG* left group entry this group drains the left apical and cardiac lobes *L 1* and *L* respectively *ACC* anterior caval channel *PCC* posterior caval channel *CD* crista dividens *A* aorta *PTr* pulmonary trunk *Az* main azygos drainage route (oblique vein of Marshall) *Oe* oesophagus

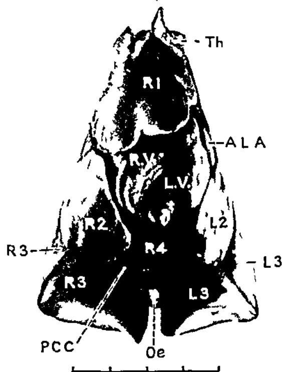
Below photograph of heart and great vessels in sternal half of same preparation *VS* via sinistra closed by its apposable portion *AP* *VD* via dextra *Az* oblique vein of Marshall which joins with the primary vein to form the coronary sinus discharging (head of arrow) into *RA* the right atrium *LA* left atrium *A and AV* aorta and aortic valve *PTr and PV* pulmonary trunk and pulmonary valve Scale in cm



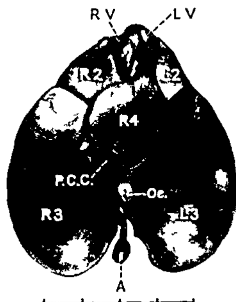
(a)



(b)



(c)



(d)

FIG 56 —Sheep foetus c 120/147 days Photographs of exsected thoracic viscera from right *a* left *b* sternal *c* and caudal *d* aspects *R 1 R R 3 R 4* right apical cardiac diaphragmatic and intermediate lobes respectively Note that *R 1* in this genus overlaps the sternal mid line *L 1 L L 3* left apical cardiac and diaphragmatic lobes respectively *P C C* posterior caval channel *A L A* auricle of the left atrium *R V* right ventricle *L V* left ventricle *P* pulmonary trunk *A* aorta *Oe* oesophagus *Th* thymus Scales in cm

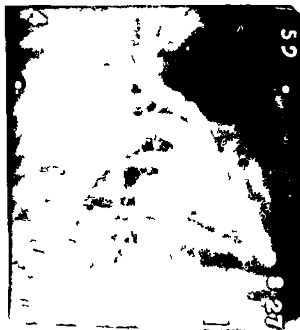


FIG 58—Sheep foetus nearly full term Frame from a direct cineradiographic record showing the filling of the left atrium and its auricle and of the left ventricle by the pulmonary venous return The shadow of the auricle is superimposed on that of the aortic valve and first part of the aorta Scale = cm on radiograph

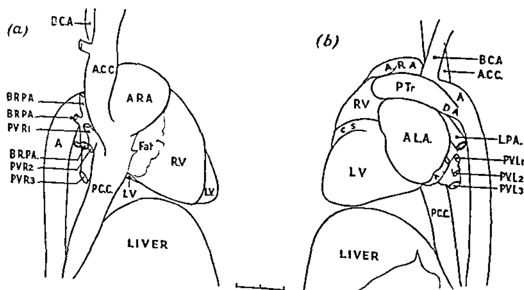


FIG 59—Sheep foetus nearly full term Outline drawings of heart great vessels etc viewed (a) from the right and (b) from the left side *PCC* posterior caval channel *ACC* anterior caval channel *ARA* auricle of right atrium *RV* right ventricle *PTr* pulmonary trunk *LPA* left pulmonary artery *BRPA* branches of right pulmonary artery *DA* ductus arteriosus *PV R1 R2 R3 L1 L2 L3* pulmonary veins draining right apical cardiac and diaphragmatic lobes and left apical cardiac and diaphragmatic lobes respectively *ALA* auricle of left atrium *LV* left ventricle *BCA* brachiocephalic artery *A* aorta *CS* coronary sulcus *A* oblique vein of Marshall (main azygos drainage route) Scale in cm

(viii) THE PULMONARY VEINS AND THE RELATIONS OF THEIR OPENINGS TO THE VIA SINISTRA (fig 57)

The pulmonary vascular arrangements are patterned by the lobation of the lungs The veins from the different lobes open into the left atrium in three groups, namely, right, caudal, and left

(1) *The right group*.—Two veins, the more cranial one from the right apical lobe and the more caudal one from the right cardiac lobe, pass separately alongside, or through into, the adipose tissue that lies between the anterior caval channel and the via dextra, i e between the two surfaces of the crista interveniens (tubercle of Lower) Before reaching the left atrium, the two veins unite and their common trunk is in very intimate relation with the dorsal and left surfaces of the more caudal portion of the via sinistra For over this part of their course the leftwards and sternally coursing pulmonary stream is separated from the more or less cranially coursing stream in the via sinistra merely by the pars libera of this channel In addition the base of the tubular via sinistra and the entry of the pulmonary venous trunk are enclosed by a marked ridge in a common surround So it would appear that the posterior caval inflow must, caeteris paribus, be reduced if the pulmonary venous return from the right apical and cardiac lobes increases, and vice versa

(2) *The caudal group*.—This is formed by two very considerable veins that drain the right and left diaphragmatic lobes respectively, and by a relatively small vein draining the intermediate lobe This third vessel opens into the vein from the right diaphragmatic lobe just before that vessel unites with the corresponding one of the left side

(3) *The left group*.—This is formed by two veins that drain the left apical and cardiac lobes respectively, they unite just before opening into the atrium

Though the veins of the right group are the ones in most intimate relation to the via sinistra, it appears probable, from a consideration of the lies of the various channels, and also from post mortem injections into the various pulmonary veins, that each of the three pulmonary inflows may impinge upon the pars libera viae sinistrae from different directions Part of the common surround for the via sinistra and right group entry is contributed by the ridge in which lies the large coronary sinus, and the caudal and left groups are separated by a minor ridge running from this main ridge

(ix) THE LEFT ATRIUM

The left atrium, like the right one, can be regarded as composed of a sinus venarum, into which various veins discharge, and an auricle, which by its structure and position is more fitted than the sinus to vary in volume Some of the lateral radiographic records (e g fig 58) give an idea of the extent of the functioning left atrium but, owing to the rotation of the heart on its long axis (see section vi above), the auricle does not show up separately in these records as that of the right atrium does in similar lateral ones (see below) This correspondence of the lateral projections of the whole left atrium and of its auricle is obvious in dissections (see, e g, fig 59*b*), for when one looks at the heart from the left side all that one can see of the atrium is its auricle, which

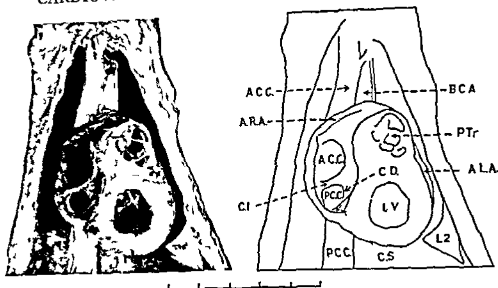


FIG 60—Sheep foetus nearly full term View of dorsal part of thorax and thoracic viscera exposed by a side to side cut in order to display the crista interveniens *CI* or tubercle of Lower *ACC PCC* anterior and posterior caval channels *ARA* auricle of right atrium *CD* crista dividens *CS* opening of coronary sinus *ALA* auricle of left atrium *LV* left ventricle *PTr* pulmonary trunk divided at level of pulmonary valve *BCA* brachiocephalic artery *L2* left cardiac lobe Scale in cm

terior caval channel,' may be defined as beginning at the accepted anatomical beginning of the anterior vena cava It inclines more and more to the right as it approaches the heart and it also bends sharply towards the sternum in the terminal part of its course (figs 60 63, 64), widening as it does so It terminates cranially at the auricle of the right atrium and caudally at the tubercle of Lower (crista interveniens)

(xiii) THE CRISTA INTERVENIENS

The term tuberculum intervenosum,' given by Lower, has two drawbacks The first is that ' tubercle " in current anatomical literature has scarcely the meaning that tuberculum ' had for Lower This difficulty led Tandler (1913) to suggest the word " torus ' as an alternative but " torus " itself is not a term in very common use The epithet intervenosum " coupled with Lower s own description implies that the tubercle is the meeting point of the anterior and posterior venae cavae, a view that one must now discard on embryological grounds The term employed by veterinary writers (Sisson, 1940) is crista intervenosa , ' crista " seems better than " tuberculum ' or torus but ' intervenosa ' is inappropriate, as already stated The name finally suggested by the present writers was " crista interveniens " i e the ridge that intervenes between the anterior caval channel and the via dextra (right terminal division of the posterior caval channel)

Lower gave a drawing of it (fig 61) viewed from the right side in the sheep and similar pronograde mammals This can be compared with a drawing of it in a foetal lamb (fig 62) It is also apparent in radiographs (figs 63 64) of

reaches up to the caudal surface of the pulmonary trunk and in so doing covers the aortic valve and the beginning of the aorta (fig 58) On its dorso caudal aspect the auricle is in direct relation to the main azygos vein (fig 59*b*) The wall of the auricle is trabeculated and between the ridges so thin as to be *translucent* The *sinus venarum is the* site of confluence of the three groups of pulmonary veins, and the tubular via sinistra of the posterior caval channel is on its medial side The main azygos vein enters the posterior wall of the sinus venarum and passes across, sternal to the pulmonary vein entries and the via sinistra, to open into the coronary sinus The course of the azygos vein and of the coronary *sinus shows up as a marked ridge on the inner surface of* the left atrium (figs 57*a*, *b*)

(x) THE LEFT VENTRICLE

There is not much that one needs to say about this chamber Viewed from *the outside (fig* 59*b*), *it is impressive*, but *its actual cavity is comparatively* small, both in the dissected specimen and also, to judge from the extent and density of the shadow of injected contrast medium (see, e g, fig 58), in the living animal From a study of all the available records, one gets the impression that the blood tends to take the shortest route to the aorta, i e that it slips round the free edges of *the atrio-ventricular valve cusps and so up into the* aorta in preference to proceeding first towards the apex This seems a very natural tendency when one studies the lie of the parts in the dissected specimen

(xi) THE ASCENDING AORTA AND ITS BRANCHES, NAMELY, THE CORONARY AND BRACHIOCEPHALIC ARTERIES

The aortic valve has shown up clearly in some of the radiographic records, and so have the beginnings of the coronary arteries Thereafter the aorta gives off only one branch before it unites with the ductus arteriosus to form the descending aorta This branch, which is of appreciable calibre (see, e g, figs 58, 18*b*), is the brachiocephalic artery, it corresponds to the human innominate, left common carotid, and left subclavian arteries and supplies mainly the head and anterior extremities Its importance from the radiographic point of view *is that it shows up when contrast blood goes* through the left side of the heart but is not outlined when such blood goes through the right side of the organ Hence it is a guide to the functional state of the via sinistra, if the injection is such that it reaches the heart through the posterior caval channel After giving off the brachiocephalic artery, the aorta is still a vessel of considerable calibre, and from 100 days (the earliest foetuses personally investigated) to full term (147 days) an appreciable flow passes through it to the *descending aorta In other* words, Kilian's concept of a separate aorta cerebralis is *quite unjustified*

(xii) THE ANTERIOR CAVAL CHANNEL

The reason for introducing the term "anterior caval channel" is similar to the third reason, given in section (v) above, for the introduction of the term "*posterior caval channel*" The canalis anterior, if one thus latinizes "an-



FIG 65 — Sheep foetus Diagram of the azygos venous drainage *A C C* anterior caval channel *O V M* oblique vein of Marshall *V M C* vena magna cordis *C.S* coronary sinus Scale in cm

third of the circumference of a circle, with its concavity facing a point somewhat to the right of the sternal mid line Dorsal to the crista is a small mass of adipose tissue, as Lower stated, it would appear to be packing deposited in a small corner that is left between various blood channels On the right side, where it faces on to the medial surface of the right lung it is more or less triangular in shape with the base of the triangle lying dorsally The relations of the various right pulmonary veins and arteries to the base are shown in fig 62 Viewed in a transverse section through the heart and lungs, it again appears more or less triangular, but this time the base of the triangle lies sternally Considered as a whole, the deposit of adipose tissue is roughly tetrahedral, it is *in relation with both* the anterior and posterior caval *channels the crista dividens*, and *the* veins from the right apical and cardiac lobes

(XV) THE AZYGOS VENOUS SYSTEM

The azygos venous drainage has been strangely *neglected* in accounts of the foetal circulation The *present* writers had *their* attention drawn to it in radiographs of injections into other systems, thereafter they examined it in detail in two fixed foetuses It is described here because all the azygos flow passes, directly or indirectly, into the right atrium, which is soon to be mentioned (section XVI below)

In the mature foetal lamb the azygos *system* is composed of three parts, namely, a caudal and a *cranial* left vein and their tributaries, and a cranial *right vein* and its *tributaries (fig 65)*

(1) *The caudal left vein* —This begins by the union of very small *right* and left branches the latter *arising* caudal to the thirteenth costo vertebral articulation *the former first* appearing half way across the vertebral *column* The common vein so formed passes up alongside *the* aorta, arches over the *root of the* left lung about the level of the fifth costo vertebral articulation *turns caudally* along the dorsal border of the left atrium perforating the pericardium in so doing, and finally unites with the vena magna cordis at the beginning of the relatively large coronary sinus At its arch this azygos *vein* is about 2 5 mm in diameter, i e it is a large vessel *for* a foetal lamb The directions of the tributaries are shown in the figure, the total number of them is sixteen, seven right and nine left

(2) *The cranial left vein* —This receives three tributaries that lie caudal to the fourth third, and *second* left ribs respectively, *it* sometimes receives a further tributary *that* lies similarly in respect of *the first rib* If it does not receive this last directly it receives its *drainage* indirectly It enters the anterior caval channel somewhat *more* cranially than vein (3) below

(3) *The cranial right vein* —This receives tributaries that lie caudal to the upper six right ribs and arches over, about the level of the first

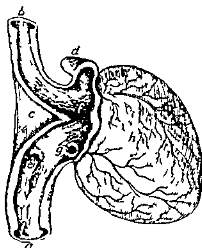


FIG 61

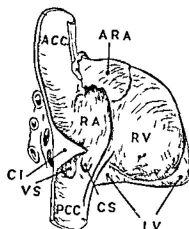


FIG 62



FIG 63 FIG 64

FIG 61 —The intervenous tubercle [crista interveniens] as pictured by Lower (1669 Plate I fig 2) in pronograde mammals *a* trunk of the ascending vena cava [posterior caval channel] *b* trunk of the descending vena cava [anterior caval channel] *c* the swelling (*tuberculum*) separating the two veins *d* right auricle *e* foramen ovale [via sinistra] *f* the opening of the heart [i e the entry into the right ventricle] *g* coronary vein [sinus] *h* the heart [i e the ventricles]

FIG 62 —Sheep foetus 140/147 days Drawing of a Lower dissection of the heart etc *ACC PCC* anterior and posterior caval channels *CI* crista interveniens *VS* via sinistra *CS* opening of coronary sinus *RA ARA* right atrium and its auricle *RV LV* right and left ventricles Scale in cm

FIG 63 —Sheep foetus 139/147 days Part of frame from direct cineradiographic record of intra vitam injection of contrast medium into jugular vein The injection has been a little too forcible and the medium has gone past the crista interveniens into the posterior caval channel Scale = cm on radiographic record

FIG 64 —Sheep foetus 135/147 days Similar to fig 63 but more contrast medium has gone past the crista interveniens Scale = 2 cm on radiographic record

foetal lambs, intravenously injected with contrast medium Finally, there is a photograph of it in a foetus fixed in situ (fig 60) In this last figure one sees the crista from the sternal aspect, and it appears as a fairly straight line sloping slightly caudally from left to right This slope emphasizes the tendency, initiated by the general direction of the anterior caval channel for the blood of that channel to go over to the right side of the atrium If one looks at the crista from the cranial aspect, it is seen not as a straight line, but as about a

(xviii) THE PULMONARY TRUNK

The term "pulmonary trunk" is somewhat of a misnomer when it is used in relation to the mature foetus For, though it gives off a large common pulmonary artery and the pulmonary circulation is an appreciable one, the main function of the trunk is to transmit the major part of the right ventricular output to the descending aorta through a ductus arteriosus which, in the living animal has a cross-section greater than the combined cross-sections of both pulmonary arteries This functional prolongation of the trunk by the ductus is also suggested by the continuity of direction of the two vessels, which is such that the ending of the one and the beginning of the other cannot be distinguished in the radiographic records Even in the fixed specimen one cannot say precisely where the ductus begins on the cranial aspect of the combined channel On the caudal aspect a common pulmonary artery is given off so one can say quite definitely where the ductus begins on this aspect The pulmonary trunk is a short vessel but a wide one, e g in a fairly large fixed foetus it was only about 2 5 cm long, but its internal diameter, before it broadened out to give off the common pulmonary artery, was about 0 7 cm In most of the radiographic records its calibre is noticeably greater than that of the first part of the aorta The tricuspid valve at the origin of the pulmonary trunk often shows up very clearly in such records (fig 25*a*)

(xix) THE PULMONARY ARTERIES

A very short distance from its origin, the common pulmonary artery separates from the ductus arteriosus and bends somewhat caudally Immediately after this it terminates by dividing into a right and a left pulmonary artery, the right one being the larger of the two In fig 50 the right artery is seen to give off two small branches just after its origin and the left artery one branch The first right branch passes round the anterior caval channel on its dorsal aspect and then goes at first cranially and then somewhat sternally, to supply the sterno cranial part of the right apical lobe As the apex of the left lung lies much more caudally than that of the right lung, this arterial branch shows up well in the lateral radiographic records (see e g , fig 17*a*) The second right branch passes dorso caudally to supply the rest of the right apical lobe It is just visible in fig 17*a* but it is perhaps unnecessary to devote any special attention to it Thereafter, the right artery gives off a branch sternally and somewhat caudally to the cardiac lobe a number of branches to the diaphragmatic lobe and a single branch caudally and somewhat sternally to the lobus intermedius The first branch of the left artery goes dorso caudally to supply the left apical lobe , as this lobe lies almost completely caudal to the pulmonary trunk the branch does not show up distinctively in the lateral radiographs Thereafter the artery gives off a single branch sternally and slightly caudally to the cardiac lobe and finally a number of branches to the diaphragmatic lobe The branches of both right and left arteries to the diaphragmatic lobes dominate the radiographic picture and if one went by this alone, one might think that there was a better blood distribution, per unit mass, to the more caudal

intercostal space, to enter the anterior caval channel about the level of the second rib

Thus the blood from ten segments (six right and four left) enters the anterior caval channel, and the blood from sixteen segments (seven right and nine left) enters the coronary sinus from a functioning oblique vein of Marshall

(xv) THE CORONARY SINUS

Into the coronary sinus discharges not only all except a negligible fraction of the cardiac venous return (the fraction being that which may discharge directly into the heart chambers), but also the major portion of the azygos venous return The sinus is, therefore, a not inconsiderable trunk, and it is surprising that the flow through it was left out of consideration in most of the earlier schemata of the foetal circulation *The course of the main azygos vein plus* coronary sinus is seen in fig 65, and fig 49 shows how the channel curves round sternal to the posterior caval channel, the ridge in which the sinus lies *helps to provide the sternal* part of the surround for the via sinistra and the opening of the right group of pulmonary veins In the last part of its course the sinus passes more or less cranially and its opening, which is devoid of a valve in the lamb, lies immediately sternal to the left part of the via dextra (fig 62) and very close to the right atrio-ventricular opening

(xvi) THE RIGHT ATRIUM

The right atrium, like the left one, can be regarded as composed of a sinus venarum and an auricle The sinus venarum includes part of the posterior caval channel, its via dextra, the coronary sinus opening, and part of the anterior caval channel (fig 62) The crista interveniens is prominent on the dorsal wall The auricle is trabeculated and between the ridges so thin-walled as to be translucent (fig 54), by its structure it is more fitted than the sinus venarum to vary in volume and, owing to the rotation of the heart on its long axis (see section vi above), it sometimes shows up clearly from the rest of the atrium in lateral radiographs

(xvii) THE RIGHT VENTRICLE

The right ventricle, like the left one, has a relatively small cavity, both in the fixed and dissected heart and also in the living animal (see, e g, fig 17*a*) Like the left ventricle, *also, it is composed of a chamber,* the walls of which are ridged by columnae carneae, and a conus arteriosus, the walls of which are smooth The left conus arteriosus, leading into the aorta shows up to a negligible extent in the lateral radiographic records, but the right one, *leading* into the pulmonary trunk, is very obvious in such records, for it lies clear of any other feature It shows considerable variations in calibre, these are doubtless to be correlated with the systole and diastole of the ventricle, but serial radiographs taken at a rate of only 3 per second are insufficient for a detailed analysis

So far as one can discover, the functioning ductus was radiographically identified for the first time in 1939 (Barclay, Barcroft, Barron and Franklin, 1939). It is perhaps unnecessary to repeat all the evidence for what was then obscure has long since been perfectly clear. The reader should however, refer back to some of the radiographs (Pl. III and fig. 23) secured during a retrograde injection into the femoral artery of a moribund foetus, and the story of the experiment may itself be of interest. The foetus, delivered by Caesarean section, was a young one of 100 days. While it was being positioned for recording, the umbilical cord broke close to the umbilicus and before the ends of the vessels could be secured so much blood had been lost that the heart-beat had become feeble and sporadic. It was thought however, that something should be done with the foetus, and the experiment rapidly decided upon was a femoral vein injection. In the hurry, the cannula was inserted into the artery instead of the vein and it looked as if the whole afternoon's work had been a dead loss. When however, the film was developed, it was found that the injection had passed right up the aorta and into the brachiocephalic and coronary arteries and via the ductus arteriosus into the pulmonary vessels. Further certain vessels had been cleared by an occasional feeble heart beat, and as a result the ductus arteriosus was very clearly defined in one frame just at the end of the run (fig. 23). So an apparently unsuccessful experiment turned out to be one of the most profitable of all.

(xxi) THE DESCENDING AORTA AND ITS TERMINAL BRANCHES NAMELY THE UMBILICAL ARTERIES

Structurally the descending aorta is a continuation of the arch of the aorta. Functionally it is a continuation of this latter and of the ductus arteriosus and the blood that it carries is derived from both ventricles either in equal amount from each or else with that from the right ventricle preponderating. Part of the blood is distributed to the trunk, various viscera, and the posterior extremities and the remainder goes via the umbilical arteries to the placenta. As pointed out by many past writers, these vessels, in the mature foetus are the large terminal branches of the descending aorta. Fig. 67a, b shows the dispositions as found in a fixed specimen. It will be noted that the right artery gives off the single caudal artery immediately after its own origin, and that a little more distal to the bifurcation of the aorta each umbilical artery gives off a vessel of small calibre. This is the internal iliac or hypogastric artery, at this stage a relatively insignificant vessel. After this the umbilical vessels pass to either side of the terminal portion of the large intestine and then converge towards the dorsal surface of the bladder. They are attached to this viscus by peritoneal folds that gradually diminish in width so that about 2.5 cm. from the umbilicus the arteries lie close against the bladder wall. Where they pass through the umbilicus they are contiguous and in the same transverse plane. In the cord they usually run a spiral course: in only one exceptional case did the present writers see them running a straight course. They are thick walled and highly contractile from a point about 3 cm. distal to their origin onwards, and from here on they shut down after ligation of the cord.



FIG 66 —Sheep foetus nearly full term (cf figs 20 and 87) View of thorax opened from the left side with cranial part of left lung and large part of pericardium removed the rest of the left lung is seen in the bottom right part of the photograph The other structures including the partially contracted ductus arteriosus can be identified by comparison with fig 59*b* Scale in cm

parts of the lungs But, if one looks back to the general arrangement of the lung masses (fig 56), one is left with the impression that the blood distribution is fairly even throughout these viscera The calibres of the arterial branches show that the blood supply can be a copious one provided the rate of flow is a high one, as will be seen in Chapter IV, this postulate is amply satisfied

(xx) THE DUCTUS ARTERIOSUS

This channel is about 1 4 cm long on its caudal aspect It terminates by *uniting with* the first part of the aorta after that vessel has given off the brachiocephalic artery It should not be described as *opening into* this part of the aorta, for in the mature foetus the two vessels are functionally comparable and of the two it is the ductus, rather than the aorta, which tends to have the greater calibre The union is a lateral one, and the rounded free edge of the "party-wall," viewed from the left side, is more or less straight except at its two ends, where it curves distally When the ductus is partially contracted instead of being full open, the free edge may be more like a letter V, with the apex of the V directed proximally There is not the least justification for Zuntz's belief (Strassmann, 1894, 406) that the party-wall, in newborn lambs, resembles a valve-like structure overlying the aortic opening of the ductus (see figs 142, 143) Nor is the post-natal closure of the ductus effected, as Strassmann (ibid, 435) thought it was, by the apposition of this "valve" over the opening

Fig 66 shows the ductus and related vessels as seen shortly after the death of a foetus, the ductus has contracted down to some extent and is already much narrower than in life This tendency to diminish in calibre under various kinds of provocation is typical of the channel in the mature foetus The histological structure corresponds, for the ductus is a "muscular" artery while the pulmonary trunk and the aorta are "elastic" vessels (Boyd, 1941, 465) The innervation of the channel has been studied mainly in non-ovine foetuses (Boyd, 1941, 467), in the lamb (Barron, 1944, 290), receptor nerve-endings of the "depressor" type are present in the adventitia near the aorta, but no fibres have been found penetrating to the muscle layer or terminating in motor type endings

GLOSSARY OF NEW NAMES FOR CERTAIN PARTS OF THE MATURE FOETAL CARDIOVASCULAR SYSTEM

Umbilical venae comites —The twin veins found in the cords of certain genera They fuse, either within the cord or else within the abdomen, to form the single umbilical vein

Sinus intermedius (formerly called "portal sinus," etc) —The intra hepatic channel uniting the umbilical vein and portal vein

Posterior/inferior caval channel (latinized as *canalis posterior/inferior*) —This is formed by the union of the posterior/inferior vena cava, the main hepatic veins and (when present) the ductus venosus It continues beyond the accepted anatomical termination of the posterior/inferior vena cava to divide within the heart, into left and right terminal divisions Blood discharges through these terminal divisions into the left atrium and right atrium respectively

The dividing ridge or *crista dividens* (formerly called "isthmus of Vieussens" "annulus fossae ovalis," etc) —The free curved caudal edge of the interatrial septum On it the posterior caval stream divides, part going to the left atrium and part to the right atrium

Via sinistra (formerly called by many the "foramen ovale") —The left terminal division of the posterior/inferior caval channel It consists of a 'fixed portion or pars firma' (usually part of the interatrial septum) and a 'free or 'apposable portion' or 'pars libera' (formerly called the valve of the foramen ovale)

Via dextra —The right terminal division of the posterior/inferior caval channel It ends cranially at the free edge of the "crista interveniens' (see below) and caudally at the free edge of the Eustachian valve (when this structure is present), i e the valve is the pars libera viae dextrae

Crista interveniens (originally called by Lower "tuberculum intervenosum" since called also 'torus Loweri, etc) —The ridge formed at the union of the via dextra and the anterior/superior caval channel (see below) when this latter is unilateral when it is bilateral the right channel alone is concerned, with the via dextra in the formation of the crista interveniens

Anterior superior caval channel (latinized as *canalis anterior/superior*) —When this is unilateral it begins at the accepted anatomical beginning of the anterior superior vena cava and ends cranially at the auricle of the right atrium caudally at the free edge of the crista interveniens When there are two channels the right hand one is as above and the left hand one is identical with the anatomical left anterior/superior vena cava

Crista reuniens (see Chapter VII section xii) —The ridge formed at the union of the ductus arteriosus and the first part of the aorta

The new terms for parts of the foetal liver i e *umbilical moiety*, *portal moiety left mass central mass* and *right mass*, are explained in Chapter VII, section (iii)

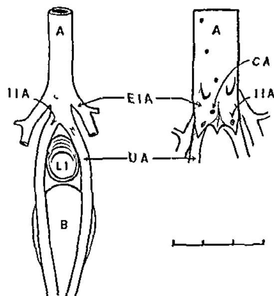


FIG 67 —Sheep foetus, 139/147 days To show that in the foetus the umbilical arteries *U A* are the large terminal branches of the aorta *A* *Left the unopened vessels right* the aorta has been opened up *E I A* *I I A* external and internal iliac arteries *C A* caudal artery L I large intestine cut across *B* bladder Scale in cm

The microscopical structure of the vessels between this point and the umbilicus was very briefly mentioned by Meyer (1914, b, 512), but only by comparison with that of the umbilical vein One imagines, however, that he would have described the arteries as follows, had he written more directly and fully about them They have a single-layered endothelium, and over most of their length no internal elastic membrane Circular muscle fibres are present throughout, and longitudinal muscle fibres are found in the distal stretches except near the umbilicus The adventitia is similar to that of the umbilical vein

The structure of the arteries of the cord was described by Popoff (1938) and by Morel and Gernez (1939) The vessels are thicker-walled than arteries of similar calibre elsewhere in the body There is no internal elastic membrane or elastic lamellae, but there are numerous anastomosing elastic fibres There is an internal longitudinal musculature, but the bulk of the media consists of layers of circular muscle, separated by elastic fibres which become less prominent from within outwards External to the circular fibres are a few oblique or longitudinal fibres, which are more and more separated by connective tissue as they get near the outside of the vessels *There is no clearly-defined* adventitia

From their own macroscopical dissections, the present writers would agree with *Morel and Gernez about the presence of some more or* less longitudinally coursing fibres on the outside, but they would be inclined to raise the question as to whether the " circular " fibres are not really " close spiral " ones

GLOSSARY OF NEW NAMES FOR CERTAIN PARTS OF THE MATURE FOETAL CARDIOVASCULAR SYSTEM

Umbilical venae comites.—The twin veins found in the cords of certain genera. They fuse either within the cord or else within the abdomen, to form the single umbilical vein.

Sinus intermedius (formerly called "portal sinus," etc.).—The intra-hepatic channel uniting the umbilical vein and portal vein.

Posterior/inferior caval channel (latinized as *canalis posterior/inferior*).—This is formed by the union of the posterior/inferior vena cava, the main hepatic veins, and (when present) the ductus venosus. It continues beyond the accepted anatomical termination of the posterior/inferior vena cava to divide, within the heart, into left and right terminal divisions. Blood discharges through these terminal divisions into the left atrium and right atrium respectively.

The dividing ridge or *crista dividens* (formerly called "isthmus of Vieussens," "annulus fossae ovalis," etc.).—The free curved, caudal edge of the interatrial septum. On it the posterior caval stream divides, part going to the left atrium and part to the right atrium.

Via sinistra (formerly called by many the "foramen ovale").—The left terminal division of the posterior/inferior caval channel. It consists of a "fixed portion" or "pars firma" (usually part of the interatrial septum) and a "free" or "apposable portion" or "pars libera" (formerly called the "valve of the foramen ovale").

Via dextra.—The right terminal division of the posterior/inferior caval channel. It ends cranially at the free edge of the "crista interveniens" (see below) and caudally at the free edge of the Eustachian valve (when this structure is present), i.e. the valve is the "pars libera viae dextrae."

Crista interveniens (originally called by Lower "tuberculum intervenosum," since called also "torus Loweri," etc.).—The ridge formed at the union of the via dextra and the anterior/superior caval channel (see below) when this latter is unilateral; when it is bilateral the right channel alone is concerned with the via dextra in the formation of the crista interveniens.

Anterior/superior caval channel (latinized as *canalis anterior/superior*).—When this is unilateral, it begins at the accepted anatomical beginning of the anterior superior vena cava and ends cranially at the auricle of the right atrium, caudally at the free edge of the crista interveniens. When there are two channels the right hand one is as above, and the left hand one is identical with the anatomical left anterior/superior vena cava.

Crista reuniens (see Chapter VII, section vii).—The ridge formed at the union of the ductus arteriosus and the first part of the aorta.

The new terms for parts of the foetal liver, i.e. *umbilical moiety*, *portal moiety*, *left mass*, *central mass*, and *right mass*, are explained in Chapter VII, section (iii).

CHAPTER IV

The Circulation in the Mature Foetal Lamb

As was stated in the last Chapter, the cardiovascular system of the mature foetal lamb is to be regarded as adequate for the needs of the moment, but at the same time certain features within it are simultaneously being prepared for the changes that are soon to occur. The circulation must be looked at in somewhat the same way, i.e. not only as a service appropriate to the foetus towards term, but also as a service which, by some rapid alterations here and there, can in a few minutes be changed to one appropriate to a very different creature, namely, the newborn lamb.

To appreciate the circulation thus defined one needs information not only about the course of the blood flow (as demonstrated, in part at least, in Chapter II above), but also about the blood, and about the development of vasomotor and respiratory mechanisms and the neuro-muscular system. So far as the lamb is concerned, the story is by no means complete, partly for a general reason (the comparatively recent development of foetal physiological research) and partly for a special reason (the lamb has not always been the experimental animal chosen for such research). However, an incomplete story is better than no story at all and its imperfections may stimulate others to emend it or to add to it. If it has those effects, its somewhat arduous composition from the literature and from the radiographic records will not have been in vain.

(i) THE BLOOD

The account which follows is derived mainly from Barcroft (1941, a, etc.) and from Barcroft and Kennedy (1939), except where otherwise stated.

Amount.—In the last third of gestation the absolute amount of blood in the placenta and umbilical cord remains more or less constant, while that in the foetus shows a great increase. The relative amounts in the placenta plus cord on the one hand, and in the foetus proper on the other hand, are as follows. At 100 days the quantities are about equal in each, at 120 days that in the placenta is about one-third of the total, and at 140 days a quarter to one-fifth. A full-term lamb, weighing between 4 and 5 kg., contains about 500 c.c. blood, and there are another 100 c.c. or more in the placenta and cord.

Ratio of cells to plasma.—This rises from about 30 : 70 at half term to 40 : 60 at full term.

Haemoglobin.—The lamb is an animal that is able to fend for itself immediately after birth, its activity at this stage contrasting strongly with the helplessness shown by the newborn of some other mammalian genera. In accord with this, the change in the nature of the lamb's haemoglobin from the foetal type (which has greater affinity for oxygen but is less able to release it) to the ultimate type takes place some time before birth (Barcroft, 1938, a, 68–70). The total amount of haemoglobin increases, in response to a physiological anoxia, from the 100th day on, and especially in the last two weeks of gestation. At 80

days the amount is only 4 g, whereas at term it is about 80 g, 67 g or so being in the foetus and 13 g in the placenta and umbilical cord

Oxygen saturation —Because of the pre-natal change in the nature of the lamb's haemoglobin and for other reasons, there is a fall in the oxygen saturation of the umbilical venous blood from over 90 per cent at about 84 days (Barcroft and Barron 1942) to 70 or 60 per cent at term (Barcroft, Barron, Cowie and Forsham, 1940 343 fig 2, Barcroft Kennedy and Mason, 1940, 352 Table II) The figures for the saturation in other vessels towards term are as follows posterior vena cava about 10 per cent (Barcroft, Barron Cowie and Forsham 1940 345) left ventricle 50 per cent or less (Barcroft, 1938, a, 38) or ± 40 per cent (Barcroft, Barron Kramer and Millikan, 1938, 43, Barcroft Kramer and Millikan 1939), and umbilical arteries 30 ± 6 per cent (Barcroft Barron Cowie and Forsham, 1940, 343, fig 2)

Oxygen content —Despite the drop in percentage saturation towards term the oxygen content of the umbilical venous blood is not correspondingly reduced, for the rate of haemoglobin formation rises in response to a physiological anoxia

Carbon dioxide —The Bohr effect, i e the shifting of the oxygen dissociation curve to the right with increased partial pressure of carbon dioxide is not specifically mentioned in the case of the lamb though it is in the case of the calf (Roos and Romijn 1938, 260) It must play an important part in the story for in the foetus the source of the carbon dioxide is the oxygen, and as the latter is used up by the tissues the former will accumulate and through the Bohr effect assist in the liberation of further oxygen With the oxygen pressure so low as it is in the mature foetus through the low percentage saturation, more attention should certainly be given to the carbon dioxide, it is surprisingly neglected in current accounts of foetal physiology

Nutrient material —While the importance of the blood gases is not denied, it should also be remembered that the umbilical venous blood carries not only fresh supplies of oxygen but also fresh supplies of nutrient material, to the foetus Little or no study of this portion of the blood content appears to have been made though it obviously should be Eisler (1930), in an otherwise somewhat uninspired note on the foetal circulation, put forward the suggestion that the nutrient material carried in the umbilical venous blood may be of even greater importance than its oxygen content

(ii) THE AMOUNT OF THE BLOOD FLOW

The cardiac output of the foetal lamb has not yet been determined, though it is very desirable that information should be available on this point In the kid which is in many ways a similar animal Barcroft, Flexner and McClurkin (1934) found that the ratio of the flow through the heart to the weight of the body varied little during the latter half of foetal life and the early post natal period It was of the order of 0 12 to 0 18 c c per g of foetus per minute If these figures are applied to the full term foetal lamb of about 5 kg in weight, they give a cardiac output of 600 to 900 c c per minute More recent determinations however, have shown that the flow through the umbilical cord alone

at term is of the order of 400 ± 200 c.c. per minute (Barcroft, Kennedy and Mason, 1939, b, 273–4), and the authors consider that the 1934 figures for the heart flow were probably *too low*, because of the errors inherent in the cardiometer itself, the shock and vascular collapse resulting from the operative interference, and the use of urethane.

Barcroft, Flexner and McClurkin (1934) reported a steady rate of oxygen consumption per g. of tissue per minute in the kid during the second half of gestation, and a marked rise after birth. Barcroft, Kennedy and Mason (1939, b) found that the *average consumption in the lamb, during the second half of gestation, was 0.0043 c.c. per g. per minute*, which is considerably less than Barcroft, Flexner and McClurkin found for the post-natal kid.

(iii) THE COURSE[1] AND RATE OF THE BLOOD FLOW

With the gradual acceptance of Claude Bernard's concept of the "milieu interne," physiologists have become more concerned with the tissue cells and the study of both respiration and circulation has been re-orientated, so that they are now regarded as the means used by these cells to preserve their activities unimpaired, either by changes in their immediate environment, or by changes in the external environment of the whole body.

In conformity with this modern attitude, the course of the blood flow in the foetal lamb (nearly full-term, unless otherwise stated) will be followed from where it leaves the tissues to where it arrives back in them. The evidence, which is *entirely, or almost entirely, radiographic, is as yet incomplete*, e.g. the circulation through certain individual parts of the body has not so far been recorded; on the other hand, the essential features have been investigated many times over, so the main part of the story is available and is indisputable. No experiments have been specifically performed to determine the rate of flow, but the radiographic records have provided a certain amount of evidence on this head and the findings are included in the account which follows.

The blood which leaves the tissues finally enters the heart by the *posterior caval channel, the anterior caval channel, and the coronary sinus*. Through the sinus, in the sheep as in a number of other mammals, there passes not only the blood returning from the heart itself, but also the greater part of the azygos venous return, and much of this return comes from the posterior parts of the body. Through the anterior caval channel flows blood coming mainly from the head and neck and fore-limbs, plus chyle from the thoracic duct, plus the smaller part of the azygos venous return. Through the posterior caval channel flows blood from the hind-limbs, the bulk of the trunk, the spleen, the alimentary canal, and the cotyledons.

One can most fittingly begin with this last, for the blood coming from the cotyledonous placenta carries the fresh supplies of oxygen and nutrient material provided by the ewe, and is therefore the most important of all the foetal venous returns. The umbilical arterial pressure is about 75 mm. Hg. and the umbilical venous pressure between 18 and 10 mm. Hg., giving a pressure gradient of about 57 to 65 mm. Hg. for the passage of the blood through the cotyledons.

[1] See plates and figures illustrating Chapter II.

Barcroft and Kennedy, 1939 181, Barcroft, Barron and Forsham, 1942) The lowness of the venous pressure was commented on by Windle (1943), who thought it was questionable if the blood reaches the heart under a greater pressure in the posterior vena cava than in the anterior vena cava The pressure gradient between the umbilical venae comites and the heart (in which, during foetal life, the pressure is presumably not sub-atmospheric) is not a very great one but as mentioned in the last section the blood flow through the cord is considerable, and the rate of flow through the venae comites is of the order of 16 cm per second (see Chapter III, section ii) At this rate, the passage through the venae comites would take 2 to 2 5 seconds, and such an estimate is supported by two radiographically determined circuit times For in one foetus contrast medium took 7 seconds to go from the umbilicus to the cotyledons and back, while in another it took 10 seconds to go from the beginning of the aorta to the umbilical vein, and a further 2 seconds to reach the posterior caval channel via this vein

Within the liver at least a ninth, and probably more of the umbilical blood passes direct to the posterior caval channel via the ductus venosus The remainder is distributed by umbilical vein offshoots to the central *and left* masses of the liver, and by offshoots of the sinus intermedius mainly to the papillary process This distribution is the afferent venous supply for about two thirds of the whole liver The other third, i e the right mass and the caudate process is supplied by portal vein blood that is much poorer in oxygen and—presumably—nutrient material, and richer in waste products *In as much* as the umbilical and portal venous distributions are quite separate, and the hepatic arterial supply is very small, there may well be biochemical differences between the umbilical and portal moieties of the liver, but experiments planned to settle this point were frustrated at the last moment, and in consequence the investigation in question remains on the list of agenda After a fairly rapid passage through the liver the bulk of the umbilical blood (that distributed to the central mass left and to the whole of the left mass) is on its way out through the left hepatic vein and the remainder (that distributed to the central mass right) together with much of the portal blood is on its way out through the right hepatic vein The rest of the portal blood reaches the posterior vena cava after an equally rapid passage through the accessory hepatic veins No information is available as to how much oxygen is lost by the umbilical blood during its intra hepatic *circuit* The relative ease with which the venous inflows pass through the liver is very noticeable in the radiographic records On the other hand these inflows are very considerable in amount and the only direct outlet via the ductus venosus, is a narrow one regulated by a sphincter that is, apparently, in an excitable condition at *term* (Barclay Franklin and Prichard, 1942 *a, c*) So it is probably safe to say that the liver is distended with blood before birth and it is conceivable that the sphincter of the ductus venosus can vary the degree of this distension

From the liver one passes to the posterior caval channel which receives four inflows of very varied degrees of venosity *The* ductus venosus blood is about 60 to 70 per cent saturated with oxygen and presumably the blood from the left hepatic vein is not very much less so On the other hand the posterior

caval blood may be only about 10 per cent saturated (Barcroft, Barron, Cowie, and Forsham, 1940, 345) That from the right hepatic vein is a mixture of roughly two parts of portal blood, which is presumably about as venous as the caval blood, with one part of umbilical blood that has made the liver circuit The effect of the union of the four flows must be to make the oxygen saturation of the combined stream appreciably less than that of the umbilical venous blood From the radiographic records it is clear that "streamlining" occurs in foetal veins as it does in post-natal veins (Franklin, 1937, 281–4), it was, therefore, conceivable that the different streams entering the posterior caval channel might have different destinations in the foetal heart, i e that one or more might go to the right side and one or more to the left side The evidence, however, that has so far been accumulated has failed to show any such differential distribution If there is no differentiation, then the oxygen saturation of the blood in the posterior caval channel must exceed that of the carotid blood, for this latter is a mixture of blood from the channel with a certain amount of more venous blood returned to the left atrium by the pulmonary veins The carotid blood is on the average about 50 per cent or less saturated and has an oxygen pressure of about 30 mm Hg (Barcroft, 1938, a, 38) That the fall in saturation is of only this order indicates that the greater part of the return to the heart through the posterior caval channel is contributed by the blood from the placenta So the channel is functionally a continuation of the umbilical vein rather than of the posterior vena cava

Within the heart, the posterior caval stream splits on the crista dividens in such a way that the bulk of the blood goes through the via sinistra into the left atrium and only a minor portion goes through the via dextra into the right atrium The anatomical dispositions favouring this unequal division have already been noted in Chapter III The extra physiological factors favouring it are the functional diminutions in calibre of the via dextra produced by (1) the coronary sinus stream, and (2) the anterior caval stream

The posterior caval blood entering the left atrium through the via sinistra is there joined by the not inconsiderable pulmonary venous return That part of this return which comes from the right apical and cardiac lobes is of particular interest, for, after passing along the dorsal surface of the crista interveniens, it flows on into the left atrium separated from the blood in the via sinistra by only the pars libera of that channel The greater part of the pulmonary return, however, is that which is carried by the caudal group of veins, i e those draining the diaphragmatic lobes and the lobus intermedius During ventricular systole and part of diastole (Westermark, 1941, 1942), excess blood entering the left sinus venarum is presumably accommodated in the readily dilatable auricle of the atrium During presystole (Westermark, ibid), the combined posterior caval and pulmonary blood passes into the left ventricle, whence it is later ejected into the ascending aorta [1] Here a small portion is distributed through the two coronary arteries to the heart muscle itself, and a much larger portion is distributed, through the brachiocephalic artery, mainly to the head and fore-limbs This left ventricular blood is more oxygenated than that from the right ventricle, but even so its degree of saturation is not a high one (50 per cent or

[1] Westermark's work is mentioned at greater length below

less, according to Barcroft, 1938, a, 38, about 40 per cent ±, according to Barcroft, Barron, Kramer and Millikan, 1938, 43, and Barcroft, Kramer and Millikan, 1939), so even the heart and brain of the foetus do not get oxygen at high pressure, as judged by post-natal standards. The residue of the left ventricular output passes on into the descending aorta.

From the radiographic records a few times have been obtained for the circuit from the brachiocephalic artery to the tissues and back to the anterior caval channel. These times are of the order of 5 to 8 seconds in the nearly full term foetus and appreciably greater in the foetus of 100 to 120 days. The series is not large enough as yet for one to decide if the decrease towards full term is characteristic. If it is, it will be interesting to discover the significance of the fall.

The blood returning to the heart through the anterior caval channel passes in its entirety to the right atrium. It is directed sternally and to the right on account of the terminal bend of the channel and the disposition of the crista interveniens. The coronary sinus flow also passes in its entirety to the right atrium. The impression that one gets from the few radiographic records in which it is visible is that this flow splays out somewhat over the wall of the atrium after it has left the sinus; presumably the wall in question is the left one but no sterno dorsal records are available to decide the point. The minor portion of the posterior caval flow that goes by the via dextra must occupy the space not taken up by the other two inflows; it is probable that it goes over towards the left side of the atrio ventricular orifice. During ventricular systole and part of diastole (Westermark, 1941, 1942) excess blood entering the right sinus venarum is accommodated in the readily dilatable auricle of the atrium; successive frames in the radiographic records show how this auricle can vary in size. During presystole (Westermark, ibid.) the combined posterio-caval, coronary sinus and anterior caval blood passes into the right ventricle whence it is later ejected along the conus arteriosus into the pulmonary trunk. After a minor, but not inconsiderable, portion has been given off to the common pulmonary artery the main portion passes on through the ductus arteriosus into the descending aorta, where it joins the residue of the blood ejected from the left ventricle.

The pulmonary vessels, as one can see from the radiographs, are not narrow ones. In addition, the average time taken by the blood to pass through the lungs is only 2.7 seconds, even before the ductus arteriosus is functionally closed (Barclay, Barcroft, Barron, Franklin and Prichard, 1942). Since the vessels are wide and the flow rapid the total pulmonary circulation is considerable. Section of the foetal lungs shows further that they contain a large quantity of blood, so the conditions obtaining justify one in styling these organs a blood depot,[1] though the conditions are not altogether similar to those described by Sjostrand (1934) in the adult, resting lungs. About the bronchial arterial supply in the foetal lamb no data, apparently, are available.

The blood in the descending aorta has a lower oxygen saturation than that in the ascending aorta. Barcroft (1938, a, 75) reported that obstruction of the

[1] The blood is not in the organ because it is being used there is Barcroft's criterion of a blood depot.

pulmonary trunk caused a much greater fall in femoral arterial pressure than did obstruction of the isthmus of the aorta, his deduction from this and from other, uncited evidence was that about a third of the blood in the dorsal aorta came from the left ventricle, and two-thirds from the right ventricle The present writers have attempted to check these figures from radiographic records of living foetuses by comparing the cross-sections of the isthmus of the aorta and of the ductus (the pressures in the two vessels must be the same, for there has never been any evidence of contrast medium passing from one to the other) If the cross-sections of the vessels were circular, then in two foetuses the blood in the abdominal aorta was derived almost equally from the two ventricles, while in the third the proportions were as in Barcroft's estimate The blood in question has a wide initial distribution to the trunk and various viscera But a large amount remains to pass through the terminal branches of the aorta, i e the umbilical arteries, and these vessels have only a few minor offshoots The flow through them is of the order of 400 ± 200 c c per minute, the pressure in them about 76 mm Hg, and the oxygen saturation in them about 30 ± 6 per cent With the umbilical arterial blood reaching the cotyledons, one is back where this story of the foetal circulation began No actual account of the passage of the blood through the placenta will be given here, for ideas of this passage are based upon knowledge of structure and not upon direct records of the flow

(iv) THE MOVEMENTS OF THE FOETAL HEART

In 1940 Franklin, Barclay and Prichard reported that the foetal lamb's heart beat in the same way as the hearts of animals of various genera studied by Bohme, i e that there was no great change in external contour but that the atrio-ventricular junction moved in turn towards the apex and the base as first the ventricles, and then the atria, contracted This statement requires some elaboration and possibly emendation Bohme learned the technique of indirect cineradiography from Janker, but increased the number of frames per second up to 150 Both Janker and Bohme used 35 mm film, which gives much more detail than the 16 mm film which has hitherto been used (in default of the 35 mm set-up) at the Nuffield Institute Bohme projected some of his excellent films at the International Congress of Physiologists, held in Zurich in 1938, and the projections left one in no doubt about the occurrence of the to and fro movement of the atrio-ventricular junction On the other hand, the exact relation of this movement to the phases of the heart's contraction could not be determined merely by watching a film projected, and one therefore accepted Bohme's spoken and written statements, based presumably on analysis of enlarged stills

The indirect cineradiographic records of the foetal lamb's heart obtained by Franklin, Barclay and Prichard, were accidental by-products of other work were few in number and, being on 16 mm film, had not the detail possessed by Bohme's records On the other hand, they showed quite definitely the lack of any marked change in external contour of the heart and (thanks to the persistence of contrast medium in the coronary vessels) the typical to and fro move-

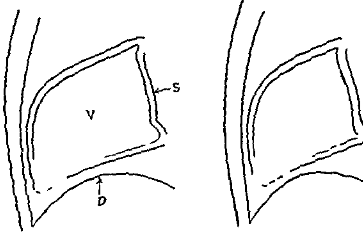


Fig 68 —(a) left (b) right Sheep foetus nearly full term Outline dra
from indirect cineradiographic record to show range of movement of
ventricular sulcus S during the cardiac cycle V ventricles D diapl

ment of the atrio-ventricular junction (fig 68a, b) It seemed reasonable, therefore to relate this movement to the atrial and ventricular contractions, i e to adopt the relation given by Bohme on the basis of his extensive researches upon adult hearts

Since then, however, Westermark (1941, 1942) has cast doubt upon this view of Bohme According to Westermark s analysis both phases o movement of the junction (first noted according to him, by Laurell) o during ventricular systole He also finds that the filling of the ventricle o during presystole only and not during the whole of ventricular diastole atrio ventricular valves in other words appear to be open only durin interval between the P and Q waves of the electrocardiogram Western speed of recording was much less than that of Bohme, but the interpret of the former s radiographic records was facilitated by the fact that simulta electrocardiographic records were available [1]

War time difficulties make it impossible to come to any final conclusio neither Bohme s nor Westermark s films are available for examination the other hand the balance is in favour of Westermark s view because h able to combine electrocardiography with cineradiography He also st the movements of the sheep s heart even if his major work was on ra hearts In the previous section of this Chapter, therefore Westermark's relations have been provisionally adopted for the foetal lamb

The lack of any marked change in external contour of the heart duri cardiac cycle requires a word or two of explanation Radiologists or a some radiologists have for a number of years been conscious that the sh the heart within the intact thorax changes less than observations made the exposed organ would lead one to believe The reason for the diff is presumably as follows No organ in the intact thorax or abdome retract away from the surrounding structures and leave a free space b them and itself for physiological conditions would, in that case b pathological ones a good example is provided by what happens in spont pneumothorax A thoracic or abdominal viscus then, though able t readily over a neighbouring viscus in virtue of the fluid layer between the

[1] Janker was the first to combine the two (Jacobi Janker and Schmitz 1932) but he d more than demonstrate the technical possibilities

pulmonary trunk caused a much greater fall in femoral arterial pressure than did obstruction of the isthmus of the aorta, his deduction from this and from other, uncited evidence was that about a third of the blood in the dorsal aorta came from the left ventricle, and two-thirds from the right ventricle. The present writers have attempted to check these figures from radiographic records of living foetuses by comparing the cross-sections of the isthmus of the aorta and of the ductus (the pressures in the two vessels must be the same, for there has never been any evidence of contrast medium passing from one to the other). If the cross-sections of the vessels were circular, then in two foetuses the blood in the abdominal aorta was derived almost equally from the two ventricles, while in the third the proportions were as in Barcroft's estimate. The blood in question has a wide initial distribution to the trunk and various viscera. But a large amount remains to pass through the terminal branches of the aorta, i.e. the umbilical arteries, and these vessels have only a few minor offshoots. The flow through them is of the order of 400 ± 200 c.c. per minute, the pressure in them about 76 mm. Hg, and the oxygen saturation in them about 30 ± 6 per cent. With the umbilical arterial blood reaching the cotyledons, one is back where this story of the foetal circulation began. No actual account of the passage of the blood through the placenta will be given here, for ideas of this passage are based upon knowledge of structure and not upon direct records of the flow.

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marked contrast to the slowness of onset, without vagal intervention, at 88 days From the 135th day onwards, under experimental conditions (i e with the uterus opened), the heart is definitely found to be under vagal inhibition in the body and in general, with such control established, the older the foetus the slower the heart rate and the lower the blood pressure During the second half of gestation the basal heart rate, i e the rate with the vagi out, is about 240 per minute and the pressure about 80 mm Hg But, with the vagi intact, the heart rate at 140, 144, and 154 days respectively was 204, 168, and 138 per minute

Ingiulla (1940[1]) found that acetylcholine injected into the jugular vein caused a fall of heart rate and blood pressure, and that stimulation of the central end of the cut vagus resulted in rise of both He also stated that the vagus of the foetus had a lower threshold of stimulation than had the maternal vagus

At 121 days Barcroft and Bauer found that an injection of adrenaline produced a rise of blood pressure associated with bradycardia Vagal ligation abolished the bradycardia which they regarded as probably a reflex, rather than a central vagal effect Possibly the carotid sinus was in action Ingiulla, on the other hand obtained a rise in both heart rate and blood pressure on injecting adrenaline

At 154 days Barcroft and Bauer found that the mechanism of the carotid sinus was established Ingiulla likewise reported that pressure changes in the foetal carotid artery gave typical sinus responses, and he concluded that the carotid sinus mechanism was in good functional order before the birth of the lamb

The cardio accelerator centre and one which is responsible for splenic contraction are also ready to play their parts at birth (Barcroft, 1938, a, 64)

The preparatory nature of many of the developments mentioned is obvious and it justifies Windle s (1943) statement that the blood circulation of the foetus is less dependent upon vasomotor mechanisms than is that of the adult

(vi) CHANGES IN THE BLOOD CONTENT OF SOME ORGANS DURING THE LATTER PART OF GESTATION

So far as they have gone studies of the course of the blood flow in immature lambs (100 to 120 days) show no great differences from the general picture obtained from studies of it in a long series of more mature lambs on the other hand certain parts of the cardiovascular system do undergo changes during the last six weeks or so of intra uterine life and these changes are of interest in connection with the phenomena of birth, so they should be mentioned at this point There is a decrease in the percentage of the total body weight that is provided by the liver from about 5 5 at 100 days to ± 3 at maturity, the percentage provided by the lungs is about 4 at 100 days, but is more or less the same as that provided by the liver at term The degrees of vascularity of the liver and lungs appear comparable If this is true, then they must hold roughly similar amounts of blood at birth About the other blood containing

[1] Not available to the present writers and therefore quoted from Windle (1943) It would be of interest to know if Ingiulla s stimulation was confined to the right vagus

only diminish its external contour if the structures with which it is in contact will yield to a corresponding extent. In the specific case of the heart, inward movements of the atria towards the interatrial septum, or of the ventricles towards the interventricular septum, are limited chiefly by the resistance of the lungs (which are the organs mainly surrounding the heart) to local stretching. One would imagine that the unexpanded foetal lung is less yielding than the expanded adult lung to pulls of such short duration as atrial and ventricular systole; further, the strength of the foetal heart muscle, if one may judge from the arterial blood pressure, is relatively less than that of the adult heart muscle. At all events, a comparison of foetal and adult cineradiographic films leaves one with the impression that the contour of the foetal heart changes less than that of the post-natal heart during the course of the cardiac cycle.

From the above consideration of the movement of the foetal heart as a whole, one may pass to a consideration of the order in which the parts contract. The evidence is admittedly scanty, and comes entirely from studies of hearts which were exsected soon after death and thereafter continued to beat. An ordinary cine film was made of the movements of one heart, so the evidence is not wholly subjective. The muscular terminal portion of the anterior vena cava contracts first, then the atria, and then the ventricles. Simultaneously with the atrial systole, there is a contraction of the free portion of the via sinistra which, as noted in Chapter III above, contains muscle fibres. Whether or not the impulses reach this musculature through the "guy-ropes" has not been decided; the experiment will be made when further foetuses become available, and ordinary cine records will be taken as required. It is realized that studies such as those mentioned above are not ideal, but it may well prove difficult, if not impossible, to follow the contractions of the via sinistra within the intact thorax.

(x) THE DEVELOPMENT OF NERVOUS CONTROL OF THE FOETAL CIRCULATION

In his book in 1938 Barcroft wrote that before birth no constant vagal tone is maintained in the foetal lamb and that towards term the heart rate is high. Since then he and Bauer have gone into the matter more thoroughly and have modified earlier views. The following is a summary of the later findings.[1]

At 88 days occlusion of the umbilical cord leads to a gradual fall in the heart rate; in this fall the vagi are not involved, and the effect is not due to abolition of sympathetic tone; it is probably the result of an action upon the pacemaker. About this time, however, it begins to be possible to demonstrate some effect of distal stimulation of the vagus nerve, i.e. reflex slowing should be possible if the stimulus is adequate. At 101 days central stimulation of the vagus is effective; asphyxia, also, can produce a vagal fall in the heart rate after a latent period of 10 seconds. At 105 days occlusion of the cord produces a vagal fall in the rate; at 119 days the rapidity of onset of this effect is in

[1] They have been made available to us before publication through the kindness of Sir Joseph Barcroft and we wish here to acknowledge our indebtedness for this courtesy.—A. E. B., K. J. F., M. M. L. P. Sir Joseph (personal communication) points out that there exist no data obtained from stethoscopic examination through the tissues of the intact ewe.

It has not been possible to determine the irritability of the ductus arteriosus in the intact, immature foetus For such a foetus is not ready to lead an independent life after interruption of the placental circulation and exposure to atmospheric temperature Hence no radiographic records are available to demonstrate the contractility of the ductus at this stage of intra uterine life There is however, some evidence obtained by other means For the ductus of a 100-days' foetus examined immediately after death of the animal may contract down very little if at all (Barclay Franklin and Prichard 1942, c) whereas that of a mature foetus, if not already fully contracted when the thorax is opened, may actually complete the process while it is under examination

There are certain vessels besides those mentioned above, which contract down after birth e g (to some extent the extra-hepatic portion of the umbilical vein and, over most of their course (to a much greater extent) the intra-abdominal portions of the umbilical arteries But about any intra uterine increase of irritability in these there is not much evidence available so one must postulate rather than prove

The converse side of the picture, i e a preparation for increased blood flow rather than for cessation of flow after birth, must presumably occur in some vessels, e g those concerned with the supply of skeletal muscles and the digestive tract, but direct evidence for this is lacking

There one could if one wished, end this account of the pre natal circulation and circulatory system in the lamb, for nothing further can be added to it from the cineradiographic records There is however certain information which has been obtained by other means and which should properly be included here if the reader is to have a better understanding not only of the circulatory system but also of the respiratory and neuro-muscular systems the activities of which cannot ultimately be separated from those of the circulatory one The extra information is to be found in various publications by Barcroft and his colleagues, and all together it forms a very considerable contribution to foetal physiology

(viii) THE OXYGEN SUPPLY OF THE MATURE FOETUS

One of the main functions of the circulatory system is to carry oxygen from the placenta to the various parts of the body To judge from the skittishness of lambs soon after birth intra uterine provisions have been entirely adequate It comes, therefore, as somewhat of a shock when one learns for the first time that

(1) The adequacy of the placental bed declines from 100 days up to term ,

(2) The change from the foetal type of haemoglobin to the post natal type (which is less suited for taking up oxygen in the placenta) takes place some time before birth ,

(3) The oxygen saturation of the blood at term is similar to that which would be found in an adult human being in the Himalayas

There are however points on the other side

(1) Towards term the blood pressure rises thus increasing the flow through the placenta ,

(2) There is increased formation of haemoglobin ,

(3) Skeletal movements and postural activity (see below) are inhibited

organ, i e the spleen, one can provide no radiographic evidence of consequence, for this viscus does not, in the foetal lamb, remove injected thorotrast from the blood and thereby show up in radiographs, post mortem, it is not very large

(vii) INCREASING IRRITABILITY OF VARIOUS FOETAL VESSELS AND CHANNELS TOWARDS TERM

Among the structures which are functionally appropriate to the circulation at term, but which, in addition, are ready to play their parts in the change-over to the post-natal circulation, are the umbilical vessels *at or near the umbilicus* various intra-hepatic venous channels, the ductus venosus, the via sinistra, and the ductus arteriosus

The umbilical vessels at or near the umbilicus are the most important in this list, for if they do not close down at or soon after birth, the lamb will obviously die On the other hand, patency of the via sinistra or of the ductus arteriosus may not have any very serious consequences (Beattie and Morton, 1939) So far as the evidence goes, the irritability of the umbilical vessels at or near the umbilicus increases towards full-term The intra-hepatic umbilical vein and its offshoots, and the sinus intermedius, may at the same time exhibit variations in calibre that one can only attribute to similar increases in irritability, a vessel may be wide *during the course of one injection and very constricted during the* course of a second one only a few minutes afterwards The different vessels do not constrict or dilate in unison, so there is no question of a variation of the blood inflow as a whole, it is just that the vessels all seem, so to speak, somewhat "jumpy" On the basis of a relatively small number of records, one would say that there are considerable individual differences in respect of this intra-hepatic irritability

The "sphincter" of the ductus venosus, though not of any great absolute width, is relatively much thicker than any musculature in the walls of the intra-hepatic vessels that have just been under discussion Its irritability increases towards term and it can exhibit rapid contractions and relaxations in a foetus delivered by Caesarean section, even though the placental circulation is uninterrupted and pulmonary respiration is prevented by a nose-bag *filled with* amniotic fluid On the other hand, the sphincter does not exhibit so high a degree of irritability in all foetuses under these conditions, so *here again there* are differences between individuals, as one might have expected

Of the irritability of the free portion of the via sinistra there is very little direct evidence available, but in at least one foetus there was a temporary closure of the via while the placental circulation was continuing and while pulmonary respiration, though not necessarily respiratory efforts, was prevented It is said that the musculature of the pars libera increases up to birth, certainly it is very obvious at term, while in immature foetuses the membrane may be practically transparent As already mentioned, the musculature of the pars libera contracts, in the exsected heart, simultaneously with the atria On the basis of these various observations, one can reasonably suppose that the pars libera is more contractile towards term, though one cannot at present state how large a part its musculature plays in the functional closure of the via sinistra

dead or at least soundly asleep It can, however, be "woken up" by asphyxia, suitable section of the brain, or exposure, and it is necessary to explain the mechanisms involved Throughout the period from the 34th day to term, the effect of asphyxia is fundamentally the same, namely, a depression of the central nervous system with the higher centres more affected than the lower ones The visible signs of asphyxia, on the other hand, change markedly in character as ever higher parts of the brain become included with the progress of gestation, in the functioning nervous system In the earlier stages the highest functioning centres are those which excite skeletal movements, so the end result of asphyxia is reduction of muscular activity In the later stages the opposite is true, for the highest functioning centres are now inhibitory ones hence the end result of asphyxia at these stages is release of the lower centres and, therefore increase of muscular activity Suitable surgical section of the brain effects a similar, but permanent, release and a foetus subjected to this procedure remains active throughout Exposure increases activity because of the increase in exteroceptive nerve impulses which takes place when the lamb is removed from its isothermic and more or less isotonic external environment i e from the amniotic fluid Directly it is so removed there is a development of muscle tone which does not normally exist in utero

The differentiation of movements in the foetus occurs as follows Up to about the 42nd day the only kind of movement is a spasm This later develops into a general spasmodic rhythm which can be divided into an initial spasm and a subsequent rhythm Later still the general spasmodic rhythm becomes an initial spasm somatic in character, with progressive and gravitational components The subsequent rhythm, on the other hand, becomes respiratory in character, and regulated in frequency and amplitude, its components are (1) respiratory rhythm and (2) labial and lingual rhythm, chewing, and sucking The response to stimulation of any particular afferent nerve is at first local later it becomes more widespread, and finally it once more becomes local

The respiratory movements at 50 days or so are incapable of drawing anything into the thorax, for the chest wall is soft and the trachea is not open Normally the movements are shallow and slow, but they are deepened and accelerated after somatic activity, oxygen lack and carbon dioxide excess do not at this stage initiate or deepen, or quicken them Between the 50th and 60th day they tend to disappear in common with other movements under the inhibitory influence of the higher centres But they can be unmasked as already described by appropriate surgical section If the cut is made below the red nucleus the respiration is gasping in type and the muscular movements jerky, if on the other hand, the cut is made above this nucleus the respiratory movements are normal in type and the somatic movements more sustained

The broad correspondence between the circulatory and respiratory arrangements in the mature foetus is obvious from what has been written, it is clear that there are present at term, not only

(1) a circulatory system functioning for the immediate needs of the organism and

(2) a respiratory system, namely, the placenta, functioning similarly, but also

during the second half of the gestation period and certain important organs (first, the umbilical moiety of the liver, and secondly, the heart, brain, thyroid and thymus) get the most oxygenated blood that is available,

(4) The foetus does not have to produce heat in order to keep up its temperature,

(5) The Bohr effect is of assistance to the tissues in obtaining the oxygen which they need,

(6) The oxygen content of the blood, as opposed to its saturation, remains fairly high, and

(7) The brain of the foetus and newborn animal is less susceptible than that of the adult to permanent damage from anoxia (see Windle, 1943)

In the full-term foetus, in consequence of these compensating factors, there is no indication of any serious degree of asphyxia which, by putting out of action the highest centres, would release the reflex muscular movements mediated through the lower centres (see below) One may, therefore, say that the functioning respiratory system in the mature foetal lamb is adequate for the immediate needs of the organism

(IX) THE DEVELOPMENT OF RESPIRATORY MECHANISMS WHICH WILL TAKE OVER AFTER BIRTH

The cardiovascular change-over at birth is effected by modifications within a system which has already been functioning up to birth The respiratory change-over, on the other hand, demands the development, during foetal life, of an entirely different mechanism from that which provides for the foetus in utero A study of this development cannot be entirely dissociated from the study of the development of the neuro-muscular system as a whole, so the following survey deals to some extent with both It is based mainly on publications by Barron and Windle (1936), by Barcroft alone (1938–1943 passim), by Barcroft, Barron, Cowie and Forsham (1940), and by Barcroft and Barron (1942, b)

In the first part of intra-uterine life, the only movements observable in the embryo are the beats of its heart Between the 32nd and 34th day, however, it becomes possible to elicit contractions in skeletal muscles by direct faradic stimulation, and about the 34th day a rather strong tap on a specific skin area, i e just below the eye, causes a reflex twist of the neck which results in a backward movement and rotation of the head The stimulus has been picked up by a branch of the fifth nerve which is still in course of development it is the sole stimulus which, at this period of the animal's growth, will elicit a reflex movement As time passes, the receptive skin-area increases in extent, the threshold of stimulation falls, and the reflex movements not only involve more muscles and last longer, but also assume more purposive characters, to which reference will be made in the next paragraph The period, during which reflex activity increases so strikingly, is one in which the spinal cord and hind-brain are developing functionally and it lasts up to about the 50th day, when the inhibitory activity of the fore-brain begins to exert a damping influence on the movements By the 70th day this influence is predominant, and immediately after exposure a foetus of this age lies without movement to all appearances

dead or at least soundly asleep It can, however, be "woken up" by asphyxia, suitable section of the brain or exposure and it is necessary to explain the mechanisms involved Throughout the period from the 34th day to term, the effect of asphyxia is fundamentally the same, namely, a depression of the central nervous system, with the higher centres more affected than the lower ones The visible signs of asphyxia, on the other hand change markedly in character as ever higher parts of the brain become included, with the progress of gestation in the functioning nervous system In the earlier stages, the highest functioning centres are those which excite skeletal movements, so the end result of asphyxia is reduction of muscular activity In the later stages the opposite is true for the highest functioning centres are now inhibitory ones, hence the end result of asphyxia at these stages is release of the lower centres and therefore, increase of muscular activity Suitable surgical section of the brain effects a similar, but permanent, release and a foetus subjected to this procedure remains active throughout Exposure increases activity because of the increase in exteroceptive nerve impulses which takes place when the lamb is removed from its isothermic, and more or less isotonic, external environment, i e from the amniotic fluid Directly it is so removed, there is a development of muscle tone, which does not normally exist in utero

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(1) a circulatory system functioning for the immediate needs of the organism and

(2) a respiratory system, namely, the placenta, functioning similarly, but also

(3) mechanisms prepared to effect the change-over of (1) to the post natal type, and

(4) a respiratory system suited to replace (2) after birth

One of the most surprising features of the whole business is the earliness of the stage at which the anticipatory mechanisms are first detectable Developmental studies are always providing one with causes for wonder, but it is certainly remarkable that an embryo, less than an inch in length, is already being prepared for an event that will not take place until about 110 days later, by which time the once minute creature will have become a sizable foetus of 3 to 5 kg in weight

(x) CONCLUDING REMARKS

There one may leave the more general story and revert to the real subject of this Chapter, namely, the foetal circulation The account of the cardiovascular system (1) functioning for the immediate requirements of the organism and (2) simultaneously undergoing developments that fit it to play its part during birth, includes practically all the exact knowledge that has been accumulated in recent years The objective records on which the story is based are so numerous that there can be no doubt about the course of the blood flow under the experimental conditions that have actually obtained The only question, therefore, is whether such findings are applicable to the foetus in utero One can answer it as follows The sole serious change from the intra-uterine conditions has been the removal of the greater part [1] of the foetus from the amniotic fluid The consequent effects of exposure of the lamb's skin to room temperature have been minimized by drying the lamb immediately after delivery, and by keeping the room as warm as possible The umbilical cord has been wrapped in dry cotton wool, and care has been taken to avoid mechanical stimulation of its contained vessels One can also point out that records, begun and completed within 30 and 60 seconds respectively from delivery, have given the same circulatory picture as records begun and ended much later On the face of it, it seems unlikely that any serious change has taken place in the circulation within half a minute of delivery by Caesarean section, so it is reasonable to suppose that the picture obtained is identical with that of the blood flow in utero

This being so, it is easy to see in what respects the various hypotheses of the foetal circulation (see Chapter I) have been at fault, e g Harvey was wrong in denying a pulmonary flow before birth, and so forth The final story has some resemblances to Sabatier's schema, as modified by Bichat, but it differs from it in an important point, for a considerable residual flow passes from the first part of the aorta into the second In the lamb, too, the anatomical basis of Sabatier's original schema, i e the Eustachian valve, is non-existent For these reasons, and also because facts are very different things from hypotheses, the present story cannot be regarded as a confirmation of Sabatier's views It stands by itself, and is in an entirely different category from the various statements that have appeared at intervals during the last three hundred years

[1] The exception has been the muzzle of the foetus from which impulses pass to evoke pulmonary respiration Over this important skin area the intra uterine environment has been artificially retained by means of a nose bag filled with amniotic fluid

CHAPTER V

The Birth of the Lamb and the Rupture of its Umbilical Cord

SOME description of the natural process seems to be required at this point, i e after the Chapter on the circulation in the mature foetus and before that on the changes which occur during and shortly after, birth It is not, however, easy to get first hand accounts of natural lambing, for those who have most practical experience i e shepherds are either not loquacious or else are not concerned much with the aspects which are of interest to the scientist The matter is further complicated by the facts that flocks vary in their habits, that natural birth differs from assisted birth, and so forth

In view of the above mentioned difficulties and of the lack of monographs devoted solely to ovine obstetrics it seems best to present here three accounts and a number of photographs The first of the accounts is a precis compiled from various scientific works (Meyer, 1914 a b, Fleming, 1930, Marshall and Halnan 1932 Williams, 1940) the second gives the personal experience of a friend Mr M J Hirst, in the Pennines and the third is from an article which was written by Mr Macdonald Hastings and which appeared in the April 4, 1942 number of *Picture Post* The illustrations are photographs which were taken by Mr Kurt Hubschman in connection with that article, and most of them have not previously been published

(1) A PRÉCIS OF SOME SCIENTIFIC ACCOUNTS

It is important to remember that the ovine placenta is of the cotyledonary type that the length of the umbilical cord varies but is often of the order of 20 to 25 cm and that the umbilical arteries are free to slide in and out of their section of the umbilical ring while the umbilical venae comites are unable to do likewise in respect of their section of it These points may, perhaps be elaborated somewhat The cotyledonary character of the placenta means that partial detachment can occur during birth without the foetus becoming asphyxiated (contrast the case of the equine foetus described in Chapter VIII) The length of the cord is such that the lamb can normally be born without simultaneous detachment of the placenta The freedom of the arteries to move in and out of the ring is of importance in the prevention of post natal haemorrhage from these vessels this freedom according to Meyer (1914, a, b) is peculiar to ruminants In ruminants in addition according to the same authority the Wharton s jelly of the cord is semi fluid and does not restrict movement of the vessels within the cord The arteries can therefore be pulled out from the abdomen into the cord or retract from the cord into the abdomen, according to circumstances The umbilical venae comites on the other hand, can retract towards the umbilical ring because of the semi fluid character of the Wharton s jelly but they cannot retract beyond this because of their firm attachments in the neighbourhood of the ring

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One of the most surprising features of the whole business is the earliness of the stage at which the anticipatory mechanisms are first detectable Developmental studies are always providing one with causes for wonder, but it is certainly remarkable that an embryo, *less than an inch in length, is already being* prepared for an event that will not take place until about 110 days later, by which time the once minute creature will have become a sizable foetus of 3 to 5 kg in *weight*

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will contain only the two obliterated umbilical venae comites According to Meyer, they are about 3 cm long and 3 mm in diameter If the cord is slit up, the arterial section of the umbilical ring is seen to be represented by a small circular opening about 4 mm in diameter lying directly caudal to the contracted veins But these are the findings 4 to 12 hours after birth, which are inserted here merely to complete the story and to show how haemorrhage is prevented from the ends of the vessels when the cord is ruptured after the birth of the lamb

The ewe licks the newborn animal and thereby cleans it The same action probably helps to remove the semi fluid Wharton s jelly remaining in the stump of the cord and, if necessary to stimulate respiration Very rapidly the lamb is able to right its head and thereafter to rise on its legs and to seek the nourishment waiting for it in its mothers mammary gland

The third stage of labour is not usually long delayed The ewe, like most other mammals (Lenkeit, 1929), is liable to devour the afterbirth unless she is deterred from so doing The advantage if any, of such placentophagia has not been determined

If there is more than one foetus, the interval between births may be from 15 minutes to 3 hours (Fleming 1930 184)

One is not really concerned in this account, with the delayed retraction of the umbilical vessels which occurs a considerable time after birth and which, in the case of the veins depends on their slow liberation from their umbilical attachments Those who are interested in this process are referred to the papers by Meyer (1914 a b)

To conclude this section one should point out that the lamb, in contrast to the new born of the human being and of many other mammals, exhibits a remarkable degree of activity very soon after birth

(i) NOTES ON LAMBING IN THE PENNINES

By M J Hirst

My experience is very limited I have assisted at only three lambing seasons and those of only one flock, of 800 Swaledale ewes (Swaledales are horned hill sheep of the Pennines) Thus much of what is written below is applicable only to fell sheep

Before lambing.—The ewes become very restless and begin wandering about looking for place in which to lamb They quite often try to get back on to the fell They choose a sheltered spot, and there appear to be fashionable resorts especially those on the fell side of the fields Moreover, popularity changes Spots formerly much frequented now have very few lambs born in them Often ewes about to lamb will try to steal other ewes lambs They lie about a lot in the chosen spot, or else lie for a few minutes get up and pasture, then lie down again, etc etc showing signs of great uneasiness

During lambing.—You can tell when ewes are lambing or about to lamb as opposed to merely taking a siesta by their position Their hind legs are not underneath the body but stretched out to the side and they stop chewing the cud The latter is an almost infallible sign and, if observed from a distance

Normal birth can be divided into three stages

(1) Contraction of the uterus and dilatation of the cervical canal

(2) Active expulsive efforts by the diaphragm, abdominal muscles, and uterine walls resulting in the passage of the foetus through the birth canal

(3) The expulsion or dropping away of the placenta and membranes, or "afterbirth"

During the first stage, the duration of which is not specified, the ewe suffers intermittently from pain and more continuously from discomfort The pain causes her to make sporadic bleats, the discomfort makes her restless and agitated If at liberty, she seeks a remote and quiet place in which she may give birth out of sight and undisturbed

According to some authorities (e g Fleming, 1930, 183), the ewe usually gives birth standing, according to others lying on her side Normally, the duration of this second stage is about 15 minutes (Fleming, 1930, 184) The usual presentation is the fore-limbs, followed by the head, but other presentations can occur If the ewe gives birth standing, the umbilical cord ruptures as the lamb reaches the ground If she gives birth lying, it ruptures as she rises from the ground In other words, the cord is weaker than the placental attachments and cannot bear the sudden strain imposed in the one case by the fall of the lamb, and in the other case by the pull necessary to lift it from the ground Rupture occurs towards the foetal rather than the placental end of the cord According to Meyer, the umbilical arteries probably rupture at points which before the traction on the cord were intra-abdominal but which during it are extra-abdominal, and the initial pull on the intra-abdominal portions as the cord is stretched is liable to cause tears in the over-lying peritoneum After the cord has ruptured, the severed ends of the arteries retract rapidly through their section of the umbilical ring (this section thereafter contracts down to a fraction of its previous size) and come to rest within the abdomen about 2 to 3 cm from the umbilicus The amount of retraction, from the point of rupture to this resting-place, is equal to about 30 to 50 per cent of the total intra-abdominal length of the vessels, and the retraction and contraction of the smooth muscle fibres result in thickening of the arterial walls Hence such haemorrhage as occurs is very slight, it may be subperitoneal or, if the ends of the arteries project through the torn membrane, intra-abdominal Arteries examined shortly after birth were found by Meyer to be contracted and empty save for small isolated clots or pockets of unclotted blood The ruptured umbilical venae comites contract up to their point of fusion within the umbilicus or abdomen, and the single vessel resulting from their fusion may contract just at its distal end or, exceptionally, throughout its length The veins in the cord also retract from their points of rupture towards the umbilical ring but cannot, like the arteries, retract through it Their contraction and retraction result in thickening of their walls, reduction in their diameters, and obliteration of their lumina Their section of the umbilical ring probably narrows pari passu with their diminution in calibre At the distal end of the single fused vein there is commonly a small blood clot not long after birth, but elsewhere in this vessel the blood is uncoagulated It is obvious from the above account that the stump of the cord shortly after birth

Fig 70



Fig 72

or description see text

NEW TERMS FOR OLD

INTRODUCED INTO THIS BOOK

Sinus intermedius (*portal sinus* etc)

Crista dividens or dividing ridge (*isthmus of Vieussens* *annulus fossae ovalis* etc) On this the posterior inferior caval channel divides, within the heart into via sinistra (*foramen ovale*) and via dextra. Free or appossable portion of via sinistra (*valve* [illegible] *foramen ovale*).

Crista interveniens (*Tubercle* of *Lower* etc). Ridge at union of via dextra and anterior superior caval channel.

Crista reuniens. Ridge at union of ductus arteriosus and first part of aorta

clean The ... a few minutes and immediately begins nuzzl... e milk

The secon... ometimes triplets—arrives any time between ... later Oddly enough—after the first lamb is bo... and the shepherd being in attendance

As soon as th... ... and on their feet, the shepherd picks them up by the forelegs ... es them—followed by the bleating ewe—to the fold The fold is a set of hurdles divided into compartments and protected from th

saves much unnecessary walking When the lambing proper begins, the ewe lies on her side and labours, jerking her head noticeably Theoretically, if she is lambing correctly, it is best to leave her to herself, but in practice on the farm which I know, and I imagine on other hill farms (where, though the ewes come off the fell to lamb, the flock can only be visited at three-hourly intervals because of the area it covers, and not at all at night), when the ewe is found lambing, the lamb is "pulled" This is because the lamb could easily be killed before it is revisited, either through "hanging" (strangulation by the muscles in the vagina) or through suffocation The usual presentation is the head resting on the two fore-legs, but one or both legs or the head may be back, and the lamb may also come breech or back first Especially with tup lambs of the horned breeds is the danger of strangulation great In some cases the horns are so developed as to cause great difficulty, or even impossibility, of lambing unassisted This is aggravated in lowland flocks of horned sheep if they have been turnipped Even if the lamb is not strangled, its head and its tongue, which in such cases protrudes, will be terribly swollen This swelling goes down within about 24 hours from birth and it appears to cause no harm

In cases where assistance is given, the protruding water-bladder bursts as the lamb is pulled The umbilical cord breaks about the time that the hind legs come free I imagine that in unassisted cases it breaks as the ewe gets to her feet to lick the lamb

I was told, but have not myself seen, that when a ewe dies the lamb dies almost simultaneously As an example, the following was quoted A ewe killed herself heaving, possibly bursting a blood vessel Two sibling lambs were at once pulled, but they were stone dead, though they had only just died If they had not recently died it could have been told, as the fleece would have rubbed off in the hands

After birth —There is only a very little bleeding If that part of the membrane bag which covers the muzzle of the lamb fails to break, the lamb will soon smother unless the ewe licks the part away or the shepherd is there to remove it Normally the afterbirth, or cleanings, comes away soon after the lambing, or the ewe may trail it about for an hour or so

(iii) LAMBING ON THE WILTSHIRE DOWNS

By Macdonald Hastings

When the flock are ready for lambing, the shepherd brings them in to a field near the farm, called the Pen Field Thenceforward, day and night, for perhaps a fortnight, he watches the flock until every ewe has lambed If no complications set in, the actual birth is absurdly uneventful

The ewe walks about pretending to feed and searching for a suitable place for her accouchement Nobody knows what factors decide her choice But, when she's satisfied—and when she's sure that nobody, not even the shepherd, is looking—she lies down, gets up, and then lies down again When she lies down for the second time, she drops the lamb with a single quick effort As the lamb falls, a bag which contains it breaks away The ewe licks the lamb



Fig 69 Fig 70

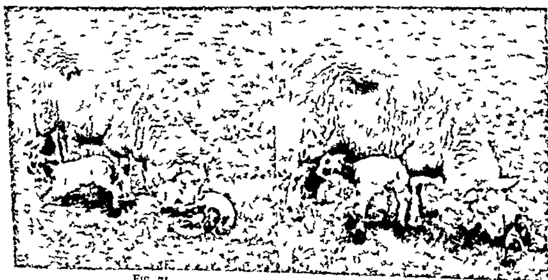


Fig 71 Fig 7

Figs 69–7.—Unassisted lambing For description see text

clean The lamb struggles to its feet within a few minutes and immediately begins nuzzling into its mother's wool to find the milk

The second lamb—there are usually twins sometimes triplets—arrives any time between ten minutes and a few hours later Oddly enough—after the first lamb is born—the ewe doesn't mind the shepherd being in attendance

As soon as the lambs are clean and on their feet the shepherd picks them up by the forelegs and carries them—followed by the bleating ewe—to the fold The fold is a set of hurdles divided into compartments and protected from the


FIG 73


FIG 74


FIG 75


FIG 76


FIG 77


FIG 78

FIGS 73-78 —Assisted lambing For description see text

weather by great wind breaks of straw Each family is put into a separate compartment, and each ewe is given a good feed of hay

When all the ewes have lambed, the shepherd turns the flock into another field bringing them in at night to the fold To wean the lambs off their mothers he separates the lambs from the sheep during the night In the morning—when the lambs are let out—there's a terrific 'to do' until all the families are united again But, day by day, the lambs become more independent At three months, they are mutton in their own right

(iv) PHOTOGRAPHS[1] OF LAMBING

TAKEN BY KURT HUBSCHMAN

Lambing as is obvious from the preceding accounts can be natural or assisted Both types are shown in the photographs which have been included as illustrations to this chapter

Figs 69–72 are of the unassisted process In fig 69 the ewe is seen standing with the first sibling ("twin) by her side In fig 70 she is lying down and the second sibling has just been born Fig 71 shows head righting just beginning in this second lamb and fig 72 shows the development of body-righting Soon this lamb will be getting up on its feet

Figs 73–78, on the other hand are of an assisted birth, in which the shepherd aids in the process Fig 73 shows the ewe lying down with her first sibling by her Fig 74 shows a fore-foot of the second lamb presenting through the dilated vulva In fig 75 the animal is nearly half born and the subsequent two figs show the completion of the delivery The umbilical cord which is seen tensed but still intact in fig 77 has been ruptured before fig 78 in which the lamb is completely separate from its mother

Finally, as a tailpiece, fig 79 is inserted In this photograph another lamb, though still with its mother and in part nourished by her, is obviously well on its way to complete independence

[1] Details stand out almost stereoscopically if one uses a magnifying glass



FIG 79 —The lamb well on the way to independence

CHAPTER VI

The Changes occurring during, and shortly after, the Birth of the Lamb

THE birth of a higher mammal is a fascinating event to watch, but the task of the moment is less to enlarge on the wonderful nature of the process than to analyse and explain, so far as possible, the changes which take place during the birth of the lamb The evidence that is at present available about the order of occurrence, and about the causation, of these changes is *derived partly from* observation of natural birth, and partly from experiment, and it will never be possible to eliminate this second source of information, because so many of the changes occur out of sight within the body Hence one will always have to assess how far experimental findings are applicable to the story of normal birth In addition, one has to recognize that there are individual differences between births, e g in the time of onset of pulmonary respiration and so forth

With these provisos, one may list certain major changes occurring during, and shortly after, the birth of the lamb as follows[1]

1 A partial change in the external environment of the lamb In utero this external environment consists of (*a*) the maternal-foetal interfaces in the cotyledonary placenta, and (*b*) the more or less isotonic, amniotic fluid The partial change mentioned is the removal of the lamb's body from the amniotic fluid at 37° C to atmospheric air and to contact with solid surfaces The consequent cooling and mechanical stimulation of the exposed body result in an immediate development of muscular activity and also cause, or aid in, the onset *of pulmonary respiration*

2 Transfer to the lamb of blood contained in the placenta and umbilical cord, provided sufficient time elapses between birth and the rupture of the cord

3 *Completion of the change in the lamb's external environment* (see 1 above) through rupture of the umbilical cord The lamb is now a separate individual

4 The onset of pulmonary respiration This may precede 3 above if the umbilical cord is compressed during the birth of the lamb

5 A rise in the lamb's arterial blood pressure, leading *reflexly to a fall in* heart rate The rise in pressure may be sufficient to establish the carotid sinus mechanism as a functioning part of the vasomotor system

6 Contraction of the spleen

7 Redistribution of the portal venous inflow to the whole of the liver instead of to only one-third of it

8 Functional closure of the sphincter of the ductus venosus

[1] No 5 must be regarded as at present somewhat sub judice (see section vi below) So far as possible Nos 1–11 are listed in their order of occurrence but the evidence is not complete e g No 7 may perhaps follow No 8 and both may be later than Nos 9 and 10

9 Functional closure of the via sinistra

10 Functional closure of the ductus arteriosus, and reduction of the pulmonary circulation time

11 In consequence of the continued development of pulmonary respiration a gradual change in the internal environment of the lamb (rise in oxygen saturation of its blood)

As a result of various combinations of the above changes

12 Establishment of the functional post natal status of the posterior vena cava

13 Attainment of functional independence by the right and left sides of the heart, with their respective arterial trunks

14 Applicability of the term ' pulmonary trunk "

15 A functional change-over in the sense that the remains of the umbilical arteries are now offshoots of the hypogastric arteries

Other changes which certainly, probably, or possibly occur are

16 Reduction by successive inspirations of the blood content of the liver

17 Redistribution of the circulating blood

18 Opening up of more capillaries

One may now pass on to describe some of these changes in greater detail

(i) EFFECTS OF THE REMOVAL OF THE FOETUS FROM THE AMNIOTIC FLUID

The exposure of the lamb s warm wet skin to atmospheric air and to contact with solid objects results in an enormous increase of exteroceptive and proprioceptive stimuli and the inhibitory activity of the higher nervous centres is correspondingly overcome This has two proved effects, one in connection with skeletal muscular activity and the other in connection with respiration (see section iv below) The former was demonstrated by Barron (see Barcroft 1935 261) who found during deliveries by Caesarean section that, so long as both the cord and the lamb were in saline at body temperature, no electrical evidence of muscular activity could be obtained So soon however, as the lamb was removed from the saline spikes appeared on the record, showing that muscle tone had been established

(ii) TRANSFER TO THE LAMB OF PLACENTAL AND CORD BLOOD

Barcroft and Gotsev (1937, see also Gotsev, 1939, and Barcroft 1941, c) compared the blood volumes of lambs born naturally with those of full term lambs which had been delivered by Caesarean section, and which had had their cords tied near the umbilicus immediately after delivery It was found that in the former animals the blood volume averaged 166 c c per kg , and in the latter only 127 c c per kg though it is possible that this second figure is too low (Barcroft 1941 c) At all events during normal birth a large proportion of the blood in the placenta and umbilical venae comites appears to be transferred to the lamb by the strong contractions of the vessels in question How strong these contractions are is shown in the Caesarean lambs if one

incises the venae comites between the placenta and the ligature, for the blood gushes out through the incisions [1]

The *amount transferred* is perhaps of the order of 80 c c (Barcroft, 1941, c) Of this about 12–16 c c could initially be in the venae comites and somewhat less in the umbilical arteries of the cord (*see Chapter III*), *the rest would have* to be in the placental vessels At the normal rate of flow in the venae comites, the transfer would take about 12 seconds (see Chapter III) The possible functional significance of the transfer is discussed in section (v) below

(iii) RUPTURE OF THE UMBILICAL CORD

In the last Chapter it was noted that the arteries probably ruptured at points which, previously to the traction, were intra-abdominal and that thereafter the torn ends retracted through the umbilical ring into the abdomen They become impervious because the inner longitudinal musculature, which is present almost as far distally as the umbilicus, thickens as the vessels retract, and is forced to encroach on the lumina of the *vessels* by the *simultaneous con* traction of the more external circular musculature Near the umbilicus the longitudinal musculature is lacking and the circular muscle contracts down over the ends of the vessels The efficacy of the arrangements is shown by the almost complete absence of haemorrhage (Meyer, 1914, a, b)

The venae comites rupture extra-abdominally and contract down up to their point of fusion They also retract within the cord towards the umbilical ring, and the combined *contraction and retraction* obliterates their lumina The umbilical vein proper, according to Meyer, may contract down at its point of origin or, exceptionally, throughout its length Personal experience has been that, in its extra-hepatic course, it is much reduced in calibre and contains little or no blood when examined some time after ligation of the cord The vessel is thin-walled, as noted in Chapter III, but its only task after *cessation* of the placental circulation is to display an activity typical of veins in general, namely, to empty itself in the direction of the heart (Franklin, 1937, 299–301), and for this its musculature is, apparently, adequate It is unlikely that the portal venous flow interferes to any extent with the process, for portal blood can scarcely reach the extra-hepatic umbilical vein in any great amount or under any great pressure during the period under review

(iv) THE ONSET OF PULMONARY RESPIRATION

As has already been noted, the great post partum *increase of afferent stimuli* can cause, or aid in, the onset of pulmonary respiration On the other hand, *such respiration* can be initiated by occlusion of the umbilical cord, occurring either naturally (pressure on the cord in the birth canal) or experimentally

[1] *The above account can be fitted in to the natural story* (see Chapter V) provided that the ewe gives birth lying down and that there is an adequate interval of time between the birth of the lamb and the rupture of the cord which occurs when the ewe gets to her feet But it is difficult to fit it in to the natural story when the ewe gives birth standing up and the cord is ruptured as the foetus falls to the ground Under these latter circumstances transfer of *blood if it occurs must be much* more rapid and must presumably be due to constriction of the placental veins and umbilical venae comites as they are exposed to sudden stretching

In the laboratory the onset through increase of afferent stimuli is the one which occurs when the ewe is delivered under local anaesthesia, i e when the foetus is in the best possible condition This observation does not however, prove which is the more normal cause of onset during natural birth for the cord is carefully protected in most experiments and is, therefore less exposed to mechanical insults The exteroceptive stimuli mainly responsible, under these circumstances, for the initiation of breathing are those evoked by the cooling and perhaps also by the drying of the muzzle of the lamb, the afferent pathways being fibres of the fifth cranial nerve But one cannot exclude the synergic effects of impulses from other cutaneous areas, or of proprioceptive impulses from the now active muscles and the joints with which they are associated These various stimuli reach centres which are ready to initiate respiration and overcome the inhibitory influence for so long exerted by the higher centres The result is the momentous first breath, one of the most spectacular of the phenomena of birth and the culmination of over a hundred days of intra uterine preparation and rehearsal In favourable circumstances this first breath is soon followed by others and, almost before one realizes it the respiration is regular and natural The lamb then begins to "wake up" and before long it makes its first bleat, sucks hard if a finger is put in its mouth rights its head then its body and finally gets on to its legs

There is at present no serial radiographic study available of the above onset of pulmonary respiration and all that one can say, from records made for other purposes is that the expansion seems to affect the trachea bronchi, and alveoli in that order and that as a result of the expansion the diaphragm shadow which is invisible at birth becomes apparent in the records It should be noted that it takes some time for the lungs to become fully transradiant in this way

If the ewe is delivered under general (urethane) rather than local anaesthesia, the nervous system of the foetus shares in the depression and the afferent impulses from the skin and elsewhere are less able or unable, to evoke the normal response (Barcroft Barron, Kramer and Millikan 1937, Barcroft Kramer and Millikan 1939) In such a case a reserve mechanism comes into play as the placental circulation diminishes This mechanism is the release of the lower centres through asphyxia of the higher ones, and the breathing which develops is of the gasping type (Barcroft Barron, Kramer and Millikan, 1938), it may continue for some time before in favourable instances, it changes into more normal respiration One imagines that the higher respiratory centres must have shared with the inhibitory centres in the depression caused by the anaesthetic and that only the lowest respiratory centre is at first capable of responding The oxygen saturation in the blood leaving the foetal brain was measured by Barcroft Barron Cowie Forsham and MacDonald (1939) who found that the level at which release takes place is remarkably constant being 15 per cent about term In a later article Barcroft, Barron Cowie and Forsham (1940) noted how small a margin exists between the actual saturation of the blood leaving the brain and the release level In contrast to the oxygen figure that for carbon dioxide was variable As the hydrogen ion level was not determined one cannot say that the release is caused by oxygen lack, but

incises the venae comites between the placenta and the ligature, for the blood gushes out through the incisions [1]

The amount transferred is perhaps of the order of 80 c c (Barcroft, 1941, c) Of this about 12–16 c c could initially be in the venae comites and somewhat less in the umbilical arteries of the cord (see Chapter III), the rest would have to be in the placental vessels At the normal rate of flow in the venae comites, the transfer would take about 12 seconds (see Chapter III) The possible functional significance of the transfer is discussed in section (v) below

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the gasps This raises the question as to whether "gasp" is the best term to use For a typical gasping respiration appears to involve constriction of the terminal bronchioles and consequently a poor gaseous interchange (Barclay, Franklin and Prichard 1940) The deep but short lasting respiratory efforts typical of the urethanized foetus after its cord has been tied must be more than gasps in this strict sense, if they so markedly and rapidly cause a rise in the oxygen saturation of the blood

To conclude this section one may revert to the blood which is transferred to the newborn lamb from the placenta and umbilical cord provided sufficient time is allowed for the process (see section ii above) The functional significance of the transfer is not yet fully clear but it raises the blood volume from about 500 c c to 600 c c or more This means that the newborn lamb has between 16 and 20 g haemoglobin per kg, a value about twice that found in the adult (Barcroft Kennedy and Mason 1939, a) In addition the blood coming from the foetal placenta is only about 60 per cent saturated, while after birth the saturation finally reaches about 95 per cent The question is whether or not the extra supply of oxygen is more than is needed for the increased metabolic activity after birth In utero the lamb is relatively *inactive* and has not to produce heat to keep up its body temperature In fact any serious degree of heat production would be a disadvantage, for the foetus has no cooling surface and extra heat would have to be dissipated by the ewe, i e still further burden would be thrown upon her circulatory mechanisms After birth, however there is a very definite need for heat production so more blood must go to the muscles and glands more is also required by other systems e g the alimentary, which before birth needed only a moderate supply for maintenance and development The view that *despite all this* the provision of haemoglobin is excessive (Barcroft, 1941, a) appears to be borne out by the fact that after birth 10 per cent or more of the lamb's haemoglobin is destroyed (Gotsev 1939 Barcroft, 1941 c) On the other hand it may be of some temporary advantage to the lamb to have the excess while the diffusion coefficient of the lungs is still low i e during the first one to five hours after birth Nor does the destruction of the 10 per cent or so of haemoglobin lead to the elimination of all the breakdown products, there is *increased* excretion of bilirubin, but the iron is apparently retained against the forthcoming needs of the organism for fresh blood formation Finally, it is possible that other constituents of the blood may be of value to the newborn lamb But so far no information is available on this head

(vi) RISE IN ARTERIAL BLOOD PRESSURE AND ITS EFFECTS

As already suggested at the beginning of this Chapter, it is somewhat difficult, on the evidence at present available to decide whether or not there is any marked increase of arterial blood pressure during normal birth

In 1888 Cohnstein and Zuntz considered that they had demonstrated a tendency for this pressure to rise even though the rise was not very great with the onset of pulmonary respiration Their experiments, however were few in number and not very convincing and the main interest of their work was that it

merely that the oxygen saturation is a very good indicator of the degree of asphyxia required. The gasping type of respiration can occur even after vagal section; on occasion it may be combined with the more normal type.

To conclude this account of the onset of respiration, one may note that breathing is usually well established within about two minutes from tying the cord (Barcroft, 1938, a, 40) and that, with the expansion of the chest, the afferent impulses affecting the process are increased by a whole new series coming from the respiratory apparatus itself—nose, throat, lungs, diaphragm and thoracic wall.

(v) CHANGES IN THE LAMB'S BLOOD AFTER BIRTH

It is convenient, though it is departing somewhat from the chronological order of events, to describe next some changes in the internal environment of the lamb, i.e. in its blood.

To begin with, one may point out that the diffusion coefficient is low at birth and for some time after because the lungs still contain a good deal of fluid (Barcroft, Kramer and Millikan, 1937; Barcroft, 1939). This explains a paradoxical effect of the exposure of the lamb to warmth (Barcroft and Millikan, 1937) and also the relatively slow attainment of a normal degree of saturation of the arterial blood with oxygen (Barcroft, Kramer and Millikan, 1937, 1939).

Exposure to warmth raises the oxygen saturation of the blood consistently, if only to a small degree. There is no hyperpnoea; indeed, respiratory activity is, if anything, reduced; the lamb tends to become sleepy. The explanation offered is that, with a low diffusion coefficient, the reduced oxygen uptake allows the blood to attain better equilibrium with the alveolar air. An exactly comparable phenomenon is seen at great altitudes, where the arterial blood darkens with muscular exertion.

The second matter is of much greater importance. It takes between one and five hours for the blood to reach its final oxygen saturation (95 per cent. or over) if the lamb breathes air (with oxygen the time is only 4 or 5 minutes). There tends to be an initial fall in saturation after the cord is tied, but thereafter there is a rise with respiration and the saturation is at a reasonable level (75 or 80 per cent.) within a few minutes from birth. Such a degree of saturation, it is true, corresponds with that of the blood of men living at great altitudes, but it is a definite improvement on the degree of saturation just before breathing begins, for this corresponds with what would be found in the blood of a man at, or above, the top of Mount Everest.

The effects of single respirations, and of groups of respirations, on the oxygen saturation of the blood were studied by Barcroft, Kramer and Millikan (1939), but their animals were not in the best possible condition, for the breathing was either a rapid shallow one with gasps superimposed, or else pure gasping. As already noted, if a foetus is delivered under local anaesthesia, it may exhibit no gasps at all, and under these conditions the oxygen saturation must be well maintained, for the lamb becomes progressively more active, bleats, gets up, and begins to run about. In animals such as those described by Barcroft, Kramer and Millikan, on the other hand, the oxygen saturation tended to fall during a series of shallow respirations and was restored only by

(viii) REDISTRIBUTION OF THE PORTAL VENOUS INFLOW

As has already been stated, it is not at present possible to say whether the taking over of the umbilical moiety of the liver by the portal inflow precedes, or succeeds or occurs more or less simultaneously with the functional closure of the sphincter of the ductus venosus Such little radiographic evidence as there is (Barclay, Franklin and Prichard, 1942, c) suggests that the process can be initiated between the onset of respiration and the cessation of the placental circulation but it is in that case associated with a deterioration of the placental flow When the portal inflow has taken over completely, one finds the calibres of the intra hepatic umbilical vein and its offshoots very much reduced, they have presumably contracted down to conform to the very much smaller amount of blood which now reaches them

(ix) FUNCTIONAL CLOSURE OF THE SPHINCTER OF THE DUCTUS VENOSUS

This requires a considerably longer description As noted in Chapters III and IV the ductus venosus of the lamb increases in size and functions as a short circuit right up to term, at its beginning there is a sphincter which may exhibit considerable irritability towards term (Barclay, Franklin and Prichard, 1942, a, c) The first discovery of this irritability was in a sense fortuitous for the Nuffield Institute team had already made an initial examination of the 1940 season's radiographic records before proceeding to an anatomical study of the foetal lamb (Franklin, Barclay and Prichard, 1940) and it was only during a re examination of the radiographs that a peculiar alternation of the ductus venosus shadow was remarked and assessed at its proper value At this point it is necessary to explain a fundamental difference that exists between ordinary experimental records and those produced by cineradiographic techniques The former are usually tracings which, within a reasonable length of time, can be *completely* analysed, the latter, on the other hand are composed of a very large number of frames and each frame is a picture that contains a wealth of detail So even with the direct method, at only three frames per second, one can never say that one has completely analysed the records and it is nearly always possible to glean some extra information by further examination It was during such a re examination that the activity of the ductus venosus sphincter was discovered (Pl V, figs 80 81 82 cf also figs 83 84)

The lamb that exhibited it (S 36) had been delivered under local anaesthesia, by Caesarean section and the record was obtained while the placental circulation was continuing and while pulmonary respiration was prevented by means of a 'nose bag' filled with amniotic fluid An injection had been made into one of the umbilical venae comites of the cord and what one noticed was an alternation in the shadow produced by the injected contrast medium, within the ductus venosus At the height of the oscillations the ductus was fully visible, invisible and then fully visible again in successive thirds of a second Finally it became completely invisible for a short while though thereafter there was a slight return of the shadow There the record of the particular 'shot' ended Fig 82 is a graph showing the fluctuations of the shadow

countered to some extent the prevailing, unverified hypothesis of a post-natal fall in pressure

Exactly half a century later, Barcroft, Barron, Kramer and Millikan reported that ligation of the cord was rapidly followed by a marked rise of pressure (about 40 mm Hg) in both the carotid and the femoral arteries, they considered that this rise was initiated by the respiratory movements but stressed that, later, some other mechanism must sustain the rise Actually, according to their fig 5, the very first increase of pressure preceded the onset of respiration, it was doubtless the direct effect of tying the cord, and it should not be confused by the reader with secondary effects consequent upon the onset of pulmonary respiration It occurs (Barcroft, personal communication, 1943) within a split second from the time the cord is clamped, the mechanism of its production is hypothetical, but precise knowledge of its causation is of little practical importance if the effect is as transient as it appears to be

Following this initial rise there were, in Barcroft, Barron, Kramer and Millikan's experiments, variations in the arterial pressure in association with respiratory movements A single movement resulted in a simple rise and fall, but a sufficiently rapid succession of movements would, the authors thought, result in a sustained rise through elimination of the troughs between individual rises There was slight cardio-acceleration with each respiration, but the variations in heart rate tended to disappear after vagal section, and the arterial pressure then stayed at a level about 25 mm Hg higher than had obtained before ligation of the cord With the vagi out of action, it was relatively easy to show the mechanical effects of respiration upon the blood pressure The authors remarked that respiration would heighten the supply of oxygen to the brain, not only through the increased uptake in the lungs, but also through the increased blood flow consequent upon the rise in arterial pressure

Two years later, however, Windle (1940, b, 25) stated that any marked rise in this pressure with the onset of respiration should be regarded as evidence of previous asphyxial depression of the foetus

An increase in pressure is often followed, in less than two seconds, by a fall in the heart rate Such slowing is not caused by asphyxia but is the end-result of an ordinary Marey's reflex, it does not take place if the vagi are cut or the arterial pressure does not show a definite rise (Barcroft, 1938, a, 49-51) Whether or not the above-mentioned immediate slowing occurs, the heart rate falls after an interval through vagus action (Barcroft, 1938, a, 54) Slowing can also be caused by a direct action of asphyxia upon the pace-maker (Windle, 1940, b, 22)

(vii) CONTRACTION OF THE SPLEEN

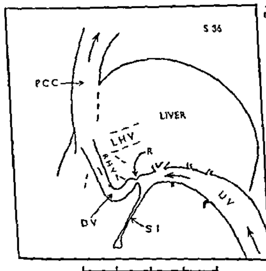
The spleen, which is innervated by sympathetic fibres only, contracts on central stimulation of the vagus (Windle, 1940, b, 22) or on tying of the cord (Taylor and Gotsev, see Barcroft, 1938, a, 56) Barcroft (1938, a, 64) postulated a medullary centre controlling the contraction, and Windle (1940, b, 24) considered that fibres from the lungs might be the afferent pathway The latter also thought that vasoconstriction might be similarly initiated



FIG 80 —Sheep foetus nearly full term Part of a frame from direct cinerad ographic record (see Plate V no 117) of an umbil cal vein injection The ductus venosus is full of contrast medium

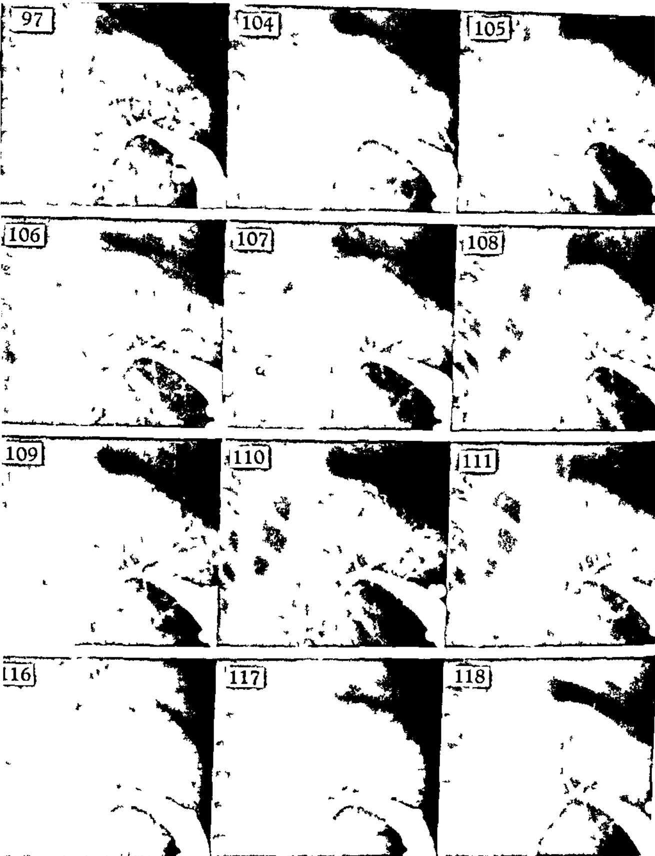


FIG 81 —Part of a frame (see Plate V no 118) immediately succeeding that reproduced in fig 80 The time interval between the two is only one third of a second but it has sufficed for the ductus venosus to become completely clear of contrast medium A stub marks the end of the umbilical vein next to the origin of the ductus venosus



KEY TO FIGS 80 and 81 —*U V* umbilical vein *S I* sinus intermedius (portal sinus) *D V* ductus venosus with lateral indentations *R* at its origin *P C C* posterior caval channel *L H V* left main hepatic vein *R H V* right main hepatic vein not very clearly defined it appears to be formed by the union of two subsidiary trunks one of which is overshadowed in fig 80 by the ductus venosus Scale = cm on radiographic record

An objective statement of the changes in the ductus and neighbouring vessels and the most probable explanation of the observed facts were given by Barclay, Franklin and Prichard (1942 a) who concluded " that the sudden constriction of the entry into the ductus venosus is the essential basis of our explanation, for if we begin anywhere else we are at a loss to account for the changes that we have noted If the above explanation is correct ' they went on then it is possible that the functional closure of the ductus venosus depends upon the irritability of a sphincter, or something similar, at the beginning of the channel combined with a fall of umbilical vein pressure, though perhaps other factors also are involved The reason why we include a fall of umbilical vein pressure



LATE V —Sheep foetus nearly full term delivered by Caesarean section Cord undivided nose bag on Parts selected frames from direct cineradiographic record of umbilical vein injection to show variation in density of tus venosus shadow Time interval between successive frames one third of a second frames shown are not all essive (see numbers on individual frames) Cf figs 80–82

of such control as still open to investigation In a more general way i e without any reference to the actual routes—nervous or otherwise—by which stimuli might reach the smooth muscle of the sphincter, they thought it possible that one or more of the following events namely, the onset of respiration the reduction of the placental circulation the detachment of the placenta and the rupture of the cord, might be directly or indirectly concerned with the contraction of the sphincter It is true that the onset of respiration was excluded in the experiment on S 36 but that result did not necessarily exclude respiration as a factor in all cases

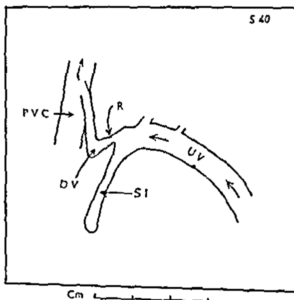


FIG 84—Sheep foetus which gave record from which fig 83 is reproduced Outline drawing made from fixed and dissected liver for comparison with fig 83 *UV* umbilical vein *SI* sinus intermedius (portal sinus) *R* ridge at beginning of *DV* ductus venosus *PVC* posterior vena cava Scale in cm

Only two foetuses (S 48 and S 49 siblings of 140 days) were available for the further experiments but the best possible use was made of this scanty material, and the technique is available for further corroborative studies when a good supply of animals is once more to hand The authors concluded as follows 'As we noted in respect of S 36, the ductus venosus can become functionally impervious after delivery of the foetus even though the nose bag is on and the placental circulation continuing Notching of the ductus [i e partial contraction of the sphincter, such as is shown in fig 83] was seen at this stage in S 48 So mere delivery of the foetus, ? with some resultant reduction of the placental circulation through cooling of the cord or contraction of the uterus, may partially or completely close the ductus If, however, this stage is prolonged and respiration is still prevented by the nose bag the ductus may reopen, as it did in a later shot (unpublished) in the case of S 36 Perhaps the initial closure, with the nose bag on was made possible by lowering of intra hepatic venous pressure through reduction of the placental circulation, and the subsequent reopening was due to deterioration of the foetus caused by continued insufficient oxygenation of the blood A factor that could conceivably be concerned —reflexly—with the increased irritability of the sphincter is the cooling of the surface of the foetus after delivery Notching or increase in notching, that occurs after the nose bag is removed, may be related to the reduction in the placental circulation that accompanies the change over from respiration via the placenta to respiration via the lungs Finally closure of the sphincter after rupture or division of the cord may be related to the still further reduction of intra hepatic venous pressure Our earlier suggestion, therefore, is not

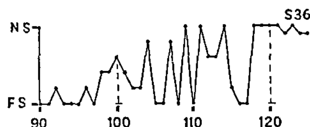


FIG 82—Graph made from direct cineradiographic record frames of which are reproduced as Plate V and figs 80 and 81 Graph begins about ten minutes from delivery of foetus Ordinates intensity of ductus venosus shadow *FS* full shadow *NS* no shadow Abscissae serial numbers of frames in cineradiographic record (rate of recording 3 frames per second)

is that we have records of a number of umbilical vein injections from three seasons of experiments, but in only two foetuses have we secured records of attempts at closure on *the part of the ductus venosus* Yet we know that normally it does so close after birth, and under such circumstances the main extra feature, absent from the umbilical vein experiments that we have quoted, is the cessation of the circulation through the cord We know, too, from our records, that the umbilical venous flow that continues for some time after delivery by Caesarean section dominates the 'portal sinus' [sinus intermedius], i e that the umbilical venous pressure, under such circumstances, normally exceeds the portal vein pressure We imagine, therefore, that the 'sphincter' of the ductus venosus may be capable of withstanding the portal venous pressure, but not the umbilical venous pressure when this is at full strength Nevertheless, we should be the first to admit that this is pure hypothesis, and merely a working explanation that has to stand or fall on the evidence produced by further research"

In 1942, the same workers attempted to find out when the channel becomes functionally impervious and what is the effective stimulus for its closure (Barclay, Franklin and Prichard, 1942, c) They were unable to produce any evidence of efferent vagal control of the sphincter, but regarded the question



FIG 83—Sheep foetus 139/147 days (*different from that which gave* records reproduced as Plate V and figs 80 81) Part of frame from direct cineradiographic record of an umbilical vein injection to show lateral indentations (notching) at beginning of ductus venosus shadow Scale = cm *on radiographic record*

of such control as still open to investigation In a more general way, i e without any reference to the actual routes—nervous or otherwise—by which stimuli might reach the smooth muscle of the sphincter, they thought it possible that one or more of the following events namely, the onset of respiration, the reduction of the placental circulation, the detachment of the placenta and the rupture of the cord, might be directly or indirectly concerned with the contraction of the sphincter It is true that the onset of respiration was excluded in the experiment on S 36 but that result did not necessarily exclude respiration as a factor in all cases

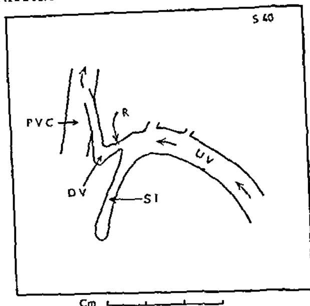


Fig 84 —Sheep foetus which gave record from which fig 83 is reproduced Outline drawing made from fixed and dissected liver for comparison with fig 83 *UV* umbilical vein *SI* sinus intermedius ("portal sinus") *R* ridge at beginning of *DV* ductus venosus *PVC* posterior vena cava Scale in cm

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immediately put out of court by our later experiments We are left with the concept of a sphincter, potentially active, that awaits merely the lowering of the venous pressure in order that it may carry out its function, namely, to render impervious the beginning of the ductus venosus channel We are not, however, in a position to say if the potential activity of the sphincter is intrinsic in the smooth muscle or is dependent on an efferent innervation The speed of contraction and relaxation of the smooth muscle, as shown in the records of S 36, is remarkable for such tissue, but can be paralleled elsewhere in the body "

The times taken for functional closure of the channel in S 48 and S 49 were between 5 and 25 minutes from ligation or rupture of the umbilical cord (figs 37, 38) These are comparable with the times taken for similar closure of the via sinistra and ductus arteriosus, for the upper limit could probably be reduced in further experiments for which less ambitious programmes were arranged

(x) FUNCTIONAL CLOSURE OF THE VIA SINISTRA

Evidence of the functional closure of the via sinistra has been obtained (1) during experiments made to determine the oxygen saturation of the carotid blood after birth (Barcroft, Kramer and Millikan, 1939) and (2) by direct and indirect cineradiography The carotid blood of lambs breathing oxygen became 95 per cent saturated with that gas within five minutes from ligation of the umbilical cord, and the attainment of so high a degree of saturation is, obviously, inconsistent with the short-circuiting of any appreciable amount of blood through the via sinistra Radiographically, one ascertains the state of the channel by making injections at intervals into one of the veins of the cord or a femoral vein, and seeing whether the contrast medium passes to both sides of the heart, or to the right side only In the former case, a shadow rapidly appears in the ascending aorta and brachiocephalic artery, showing that the via sinistra is still pervious From a study of the results, it is clear that closure of this foetal channel can occur even before the cord is tied, provided that pulmonary respiration has begun The shortest time that has been noted between the entry of air into the lung and the closure of the channel has been 5 5 minutes, at 3 5 minutes it was fully open This particular lamb was not in the best possible condition, for the ewe had been anaesthetized with urethane, so normal closure may occur even earlier It is of interest to note that the ductus arteriosus was still patent when the via sinistra was closed Closure is by no means always so rapid as in the instance quoted, and after being closed for some time the channel may reopen if the foetus deteriorates But in a healthy foetus the process is rapid and the effect permanent

The manner of the closure is of some interest Fig 55 shows the appearance of the tube in the fully open condition, as revealed during dissection of a fixed foetus Fig 85b, on the other hand, shows the appearance in another specimen in which functional closure was complete When this channel was reopened to its full extent by a probe, the picture changed to that shown in fig 85a To pass from the condition in fig 85a to that in fig 85b, the free end of the pars libera has to be telescoped back into the body of the tube, the middle part to be

pressed in towards the mid-line of the heart, and the remainder to be pressed back towards the bifurcation of the posterior caval channel The three movements are readily demonstrated on the actual specimen and are impressive not only on account of their neatness and simplicity, but also on account of the spectacular disappearance of the relatively large tube which a second before was the most prominent feature in the left atrium Fig 86 shows the via sinistra of yet another foetus (*a*) nearly fully open and (*b*) nearly fully closed The guy ropes that are so characteristic a feature of the lamb's via sinistra would appear to be too long to be concerned with its closure, i e they do not act to prevent the free end of the pars libera from passing too far back into the body of the tube Barclay and Franklin (1938) examined the heart of a lamb about 11 hours after normal birth and found the free edge of the pars libera lightly adherent to neighbouring parts, it was readily detached by a fine probe

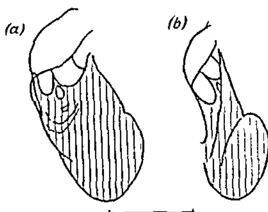


FIG 85 —Sheep foetus age unknown Drawing of the open (left) and functionally closed (right) via sinistra viewed from the left side to show how the free or apposable portion effects this closure Description in text Scale 1 cm

The efficient cause of the closure is at present hypothetical, but the structure

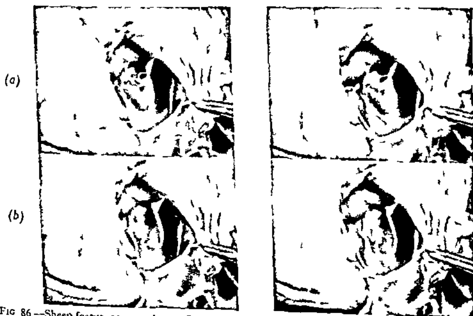


FIG 86 —Sheep foetus 139 147 days Stereophotographs of part of the heart viewed from the left side with the auricl of th left atrium removed Above the tubular via sinistra nearly fully open and below nea ly fully clos d Note the fenestrat ons at the free end of the tube and the cords or guy ropes passing across to the atrial wall

of the channel in the limb favours the idea of a mechanical rather than a neuro-muscular process and, as seen above, there is a connection with the onset and continuance of pulmonary respiration. Further, the veins returning blood from the right apical and cardiac lobes share with the via sinistra a common opening into the left atrium, so the inflow from the former can increase, caeteris paribus, only at the expense of the inflow from the latter (Franklin, Amoroso, Barclay, and Prichard, 1942). In addition, experiments carried out upon exsected hearts suggest that the streams from the caudal and left groups of pulmonary veins also take a part in the closure by playing upon the pars libera of the via sinistra. One may, then, advance the hypothesis that the closure is immediately due to increased pulmonary venous return induced by the onset of respiration, the source of the extra blood being the vascular bed of the lungs, which is gradually reduced to its post-natal capacity as successive respirations increase the air entry into those organs. This actually seems to be the only possible explanation, or at least the only possible one in some cases, in view of the fact that the via sinistra can close before the cord is tied and while the ductus arteriosus is still patent. Continuance of the closure after the initial period must be due to increased pulmonary venous return effected, in more lasting fashion, by increased blood flow through the whole pulmonary circuit.

(xi) ESTABLISHMENT OF THE FUNCTIONAL POST-NATAL STATUS OF THE POSTERIOR VENA CAVA

As a result of the cessation of the placental circulation, of the various changes in the liver, of the closure of the via sinistra, and of the redistribution of the circulating blood volume so that the now active parts can get their proper share, the posterior vena cava acquires its post-natal functional status and the term "posterior caval channel" is no longer necessary for its terminal portion plus the intra-cardiac continuation of that portion. There is presumably a widening of the vein caudal to the diaphragm, and henceforward it is the trunk into which the hepatic veins discharge as tributaries, and not another vessel with which they unite as equals. The blood from the trunk now goes to the right side only on arrival at the heart.

(xii) FUNCTIONAL CLOSURE OF THE DUCTUS ARTERIOSUS

The closure of the ductus arteriosus, as Gerard (1900) pointed out, occurs in two stages, namely, a physiological occlusion that takes place very soon after birth, and an anatomical occlusion that requires a very considerable time for its completion. In this, of course, it is paralleled by the closures of other foetal blood channels already mentioned above. The ductus is much more muscular than the vessels which it unites, and its fibres are arranged in such a way that they can be called a potential sphincter (Boyd, 1941). It has some innervation, but the full details are not yet available, and on the basis of present knowledge one should probably be guarded in one's opinions as to whether or not the channel can be looked upon as part of the vasomotor system, i.e. its closure may perhaps be a purely muscular effect rather than a neuro-muscular one. Barcroft in 1938, i.e. in the comparatively early days of research upon the

problem considered that it was the latter, and wrote " that the whole neuro-muscular mechanism has been organized in the foetus but, as far as is known, never used in the foetus that it springs into action at birth, and having performed its function, it degenerates It seems in fact to form a remarkable example of anticipation "

Evidence of its closure in lambs has been obtained in three ways

(1) Barcroft and Barron (see Barcroft, 1938, a) took foetuses with a good circulation, killed them with injections of formalin, and examined the state of the ductus in each of them They found that it was wide open and had a lumen commensurate with that of the arch of the aorta On the other hand, in a series of newborn lambs killed between 15 minutes and 2 hours from ligation of the cord one ductus was wide open one was half closed seven were contracted but not completely closed and one was completely closed "Yet who would say what relation these findings bore to the conditions before death It would be difficult, and possibly very misleading to judge of the precise condition of the cardiac sphincter before death from its post mortem appearance (Barclay, Barcroft, Barron, Franklin and Prichard, 1941)

(2) By means of blood gas determinations, for with the ductus open the blood in the dorsal aorta (umbilical artery) is more venous than that in the arch of the aorta (carotid artery)

(3) By means of direct and indirect cineradiography, combined with intravascular injections of radio opaque media (Barclay, Barcroft, Barron and Franklin, 1939 Barclay, Barcroft Barron Franklin and Prichard, 1941)

In as much as method (3) was not only less laborious than methods (1) and (2), but also gave precise information the rest of the story may be confined to the cineradiographic results Before the work began there had never been a radiographic identification of the ductus arteriosus and it was incorrectly identified during the season 1938, with consequent mis statements in four publications (Barclay Barcroft Barron and Franklin, 1938, a b, c, Barclay and Franklin, 1938) Fortunately the error was discovered, and in a further publication (Barclay Barcroft, Barron and Franklin 1939) the true story was presented The ductus was identified in three ways these have already been described in Chapter II so the evidence need not be repeated here The method finally adopted for the determination of the patency or non-patency of the channel was as follows Small injections of a contrast medium (35 per cent perabrodil) that rapidly disappears from the circulation are made at intervals into a jugular vein The medium passes in its entirety to the right side of the heart and appears in the pulmonary arteries *and* descending aorta while the ductus is open but in the pulmonary arteries alone when the ductus is closed (figs 24 25)

The intermittent records obtained in the above way show that closure of the ductus unlike closure of the via sinistra has never been apparent before ligation of the cord Nor has it ever been found to precede closure of the via sinistra, though the converse has been true in a number of foetuses It seems probable, therefore that closure of the ductus normally follows closure of the via sinistra, cessation of the placental circulation being a necessary preliminary The



Fig 87—Lamb c 11 hours post partum (cf fig 66) View of thorax opened from the left side with cranial part of left lung and the pericardium removed the rest of the left lung is seen in the bottom right part of the photograph (note light colour as compared with that of lung in fig 66) The other structures including the fully contracted ductus arteriosus can be identified by comparison with fig 59*b* Scale in cm

closure takes place within a matter of minutes from ligation of the cord, in one instance it had occurred within 4 minutes, but it may take considerably longer, and it may be preceded by a period during which there are oscillations in the calibre of the channel If the foetus deteriorates, a closed ductus may reopen, but it is safe to assume that in a healthy birth the closure is rapid, complete, and lasting The radiographic evidence is insufficient to decide whether the process begins at one or other end of the channel, or occurs more or less evenly throughout its course When it is complete, a stub marks the junction of the pulmonary trunk and the ductus (fig 260), and the average pulmonary circulation time has dropped from its foetal value of 2 7 seconds to its new one of 1 4 seconds (Barclay, Barcroft, Barron, Franklin and Prichard, 1942) The macroscopic appearance of the functionally closed ductus is shown in fig 87 (cf the partially closed ductus shown in fig 66)

(xiii) OTHER CHANGES IN THE CIRCULATORY SYSTEM

(1) After the cessation of the umbilical venous inflow, the liver can no longer be so distended, and its volume is perhaps still further reduced by the first and some succeeding inspirations At all events, the total weight of the liver falls after birth, and the normal effect of inspiration in adult animals is to expel blood from the organ (Franklin and Janker, 1937)

(2) After closure of the ductus arteriosus, the term 'pulmonary trunk' (which was a misnomer while less than half the blood in the vessel went to the lungs) becomes appropriate

(3) After closure of the via sinistra and ductus arteriosus, the right and left sides of the heart, together with their respective arterial trunks, attain their post-natal functional independence

(xiv) CONCLUDING REMARKS

There one may leave the detailed consideration of the circulatory changes that take place during the birth of the lamb But one ought not to close without some expression of admiration for the mechanisms that so smoothly effect the

transition from the pre natal to the post natal condition The sentiment is not a new one for Galen, who first described the via sinistra and ductus arteriosus, found the closures of these foetal channels more wonderful even than their original creation,[1] and it is worth remembering that he did so nearly fifteen centuries before the foetal circulation was first mentioned, and nearly eighteen centuries before the mysteries of the post natal functional closures were, in part at least, elucidated

[1] Mihique videtur multo majus esse naturam ubi quid plus in embryis quam in perfectis effecit id ipsum quando nullius amplius sit usus corrumpere quam illud omnino effecisse —Kuhn III 514

PART FOUR

COMPARATIVE STUDIES (EXCLUSIVE OF HUMAN ONES)

CHAPTER VII

Comparative Anatomy

IDEALLY, one would like to ascertain the course of the foetal blood flow in a large number of genera in the way that one has already done so in the lamb and, to some extent (see Chapter VIII), in the kid. There are, however, limitations to the use of the techniques employed. In the first place, the mature foetal lamb is near the maximum size suitable for serial radiographic recording. In the second place, some animals are too rare, or too expensive, for experimental work. In the third place, the umbilical cords in some species are too short. Fourthly, in the cases of very small foetuses, it would be impossible to insert cannulae into the veins, or at all events to insert them within a sufficiently short time from delivery. To these limitations, which are valid at all times, one must add the special war-time one, namely, the difficulty of getting any animals at all for ordinary research. Hence both the permanent, and also the temporary, value of comparative anatomical studies. For in the foetal lamb structure has been correlated with function and, if one can find in other foetuses anatomical arrangements



Fig. 88.—Red kangaroo (*Macropus rufus*) pouch specimen. Scale in cm.

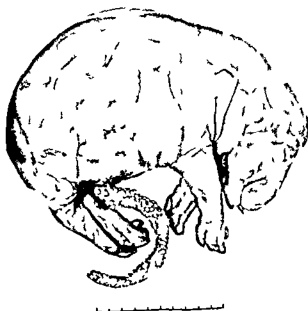


Fig. 89.—Hippopotamus (*Hippopotamus amphibius*) foetus age unknown. Note protuberances on surface of umbilical cord (cf. fig. 109 c). Scale in cm.

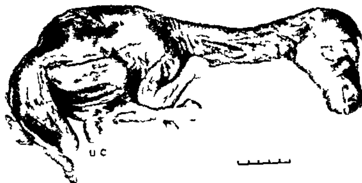


FIG 90 —Arabian camel (*Camelus dromedarius*) foetus age unknown U C umbilical cord Scale in cm

similar to those found in the lamb then one has some justification for presuming that the course of the blood flow, too, may be similar in these other animals In as much therefore as generalizations are the outcome most to be desired individual notes are largely confined to illustrative examples,

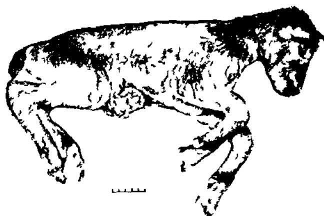


FIG 91 —Caucasian wild goat (*Capra caucasica*) foetus ? full term Scale in cm

though a few are included because they suggest lines of further, explanatory research [1]

[1] La *mecanique cachee dans une certaine espece ou dans une structure commune se developpe* dans un autre espece ou dans une structure extraordinaire & l on droit presque que la Nature à force de multiplier & de varier ses ouvrages ne peut s empecher de trahir quelquefois son secret —*Hist Acad Roy Soc Paris* 1699



FIG 92 —Malay tapir (*Tapirus indicus*) foetus stillborn Scale in cm

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FIG 88 —Red kangaroo (*Macropus rufus*) pouch specimen Scale in cm

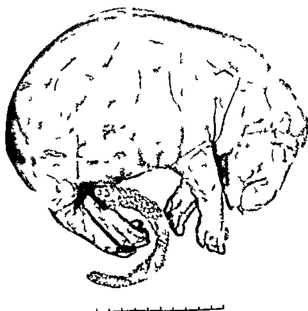


FIG 89 —Hippopotamus (*Hippopotamus amphibius*) foetus age unknown Note protuberances on surface of umbilical cord (cf fig 109 *c*) Scale in cm

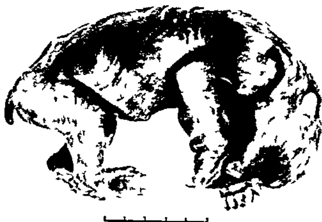


Fig 95—Brown bear (*Ursus arctos*) 48 hours post partum Scale in cm



Fig 96—Tiger (*Felis* or *Panthera tigris*) foetus age unknown Scale in cm

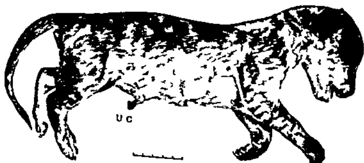


Fig 97—Lion (*Felis* or *Panthera le*) cub c 4 hours post partum U C umbilical cord Scale in cm



Fig 93—African elephant (*Loxodonta africana Elephas africanus*) foetus ? about half term Scale in cm

The account which follows in-cludes relatively few references t previous work, not because th literature has been neglected, bu because previous writers lacked th functional outlook upon structur which results from radiographi studies of the living foetus Excep in the cases of certain domestic an farm animals, the material person ally examined has been somewh fortuitously accumulated Henc the varying ages of the specimen (or sometimes complete lack o information as to age), and th *inclusion of some early post-nat* examples Some idea of the rang of the material is given by figs 88–98, and further details are to b found in the text On the other hand, it has seemed inadvisable t list all the specimens, for they ru into hundreds, largely through the numbers of ovine, bovine, and equin foetuses that have been studied Gestation times are given where they ar known and where they appear to be pertinent, but it has not seemed usefu to include them where knowledge is insufficiently precise or where the ages of the foetuses themselves are unknown, those interested, however, can find a summary of many of the available data in Needham (1931) vol 1, Tables 6 and 63, and in Kenneth (1943) The mammalian classification used is that given in the Centenary List of the Zoological Society of London (see Flower, 1929), not because that classification is necessarily final, but because the book is reasonably accessible and because a number of the specimens have come from the Society's Gardens in London or from Whipsnade

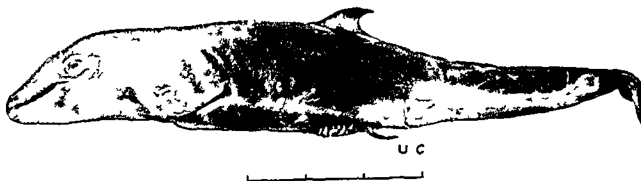


Fig 94—False killer whale (*Pseudorca crassidens*) foetus age unknown *U C* umbilical cord Scale in 10 cm

The anatomical features will be discussed in the following order

(i) The placenta
(ii) The umbilical cord and the umbilical vessels
(iii) The liver
(iv) The ductus venosus
(v) The posterior caval channel and its terminal bifurcation
(vi) The via sinistra and its pars libera
(vii) The via dextra
(viii) The lobation of the lungs, the pulmonary veins and the relations of their openings to the via sinistra
(ix) The anterior caval channel and its relation to the via dextra, the crista interveniens
(x) The azygos venous system and the coronary sinus
(xi) The apex of the heart
(xii) The pulmonary trunk and the ductus arteriosus

(i) THE PLACENTA

Mossman (1937) defined the normal mammalian placenta as "an apposition or fusion of the fetal membranes to the uterine mucosa for physiological exchange" What is commonly called 'the placenta in eutherian mammals is more correctly speaking the chorio-allantoic placenta It comes within the scope of the above definition but is not the only structure which does so, and it was therefore more closely defined by Mossman His definition, modified to avoid a teleological phrase contained in it may be given as follows The chorio allantoic placenta is a portion of the chorion vascularized by allantoic vessels it is intimately apposed to or fused with the uterine mucosa and it serves as a medium for physiological exchange In the rest of this section the structure in question will be styled the placenta and will not be qualified by the epithet chorio allantoic

Placentae were earlier classified according to their gross shape, and their non-deciduate or deciduate character (semi placenta and placenta vera respectively in Strahl s terminology) The non deciduate placenta separates in the third stage of labour without simultaneous removal of maternal tissue the deciduate carries with it because of its more intimate association with the uterine wall, a variable amount of maternal tissue For a number of reasons, classification according to gross shape, etc , is unsatisfactory on the other hand the gross shape is an obvious feature of any particular placenta and should be noted in the full description of it The four principal forms have therefore been illustrated in figs 99*a* 100*a* 101, and 102 The diffuse is that found in the horse and pig the cotyledonary (or multiplex, in Grosser s terminology) that in the ovine and bovine, the zonary that in the cat and dog and the discoid that in the guinea pig

Another distinction between placentae, but this time one based upon their finer structure, separates them into labyrinthine and villous Here, again, the type found should be noted in the full description of any particular placenta,



FIG 98—Gorilla (*Gorilla gorilla*) foetus ? full term Note umbilical cord in frontal view Scale in 5 cm

maternal endothelium and the foetal trophoblast connective tissue and endothelium The gross shape ranges from zonary to discoid and the endometrial relation is deciduate Placentae of this type are found in carnivores

(4) *The haemo chorial* — The membrane comprises the foetal trophoblast, connective tissue and endothelium i e maternal blood is in direct contact with the trophoblast The gross shape is discoid and the endometrial relation is deciduate Placentae of this type are found in insectivores bats primates, and lower rodents

(5) *The haemo endothelial* (Mossman s addition to Grosser s classe) The

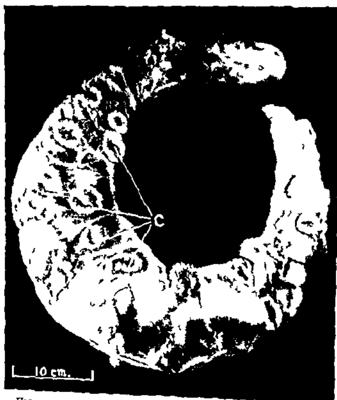


Fig 100*a* —Bovine foetus within its membranes removed from the uterus at the *100th* day of pregnancy showing cotyledons C on the surface of the chorion

membrane consists of the foetal endothelium alone, i e this layer alone separates the maternal blood from the foetal blood The gross shape is discoid, cup-shape, or spheroidal, and the endometrial relation is deciduate Placentae of this type are believed by Mossman to exist in higher rodents, such as rabbits, pocket-gophers, kangaroo-rats, mice, rats, and

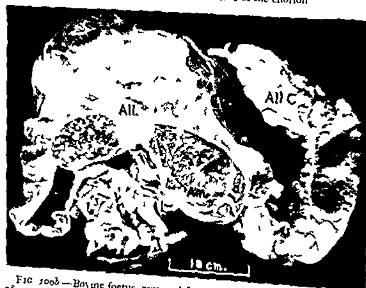


Fig 100*b* —Bovine foetus removed from the uterus at about the 100th day of pregnancy with the chorion *partially* dissected away to show the shape of the allantois *All* and the amniotic pustules on the surface of the amnion *Am* All C part of the *allanto chorion* with cotyledons on the outer surface of the chorion

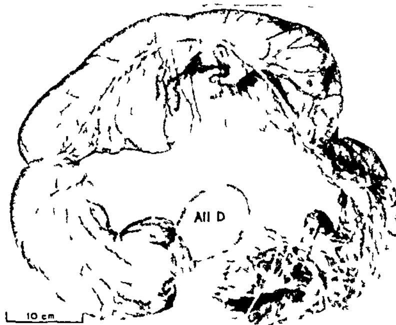


FIG 99a —Pig foetus within its membranes removed from the uterus at the 80th day of pregnancy Unfortunately the ridges in the chorion are not well seen *All D* allantoic diverticulum

but the distinction is insufficient basis for any real system of classification

In fact, the only system which has given any reasonable degree of satisfaction is that put forward by Grosser (1927) and later (1937) slightly modified by Mossman It is based upon " the intimacy of contact between the chorion (trophoblast) and the maternal tissues and thereby indicates the thickness and constitution of the membrane separating the maternal and fetal blood-streams, that is, the placental membrane " The resulting classes (figs 103–106, 147) are five in number

(1) *The epithelio-chorial*, in which the membrane comprises, on the maternal side endothelium, connective tissue and epithelium, and on the foetal side uterine lumen, trophoblast, connective tissue and endothelium The gross shape is diffuse and the endometrial relation non-deciduate Placentae of this type are found in the horse and pig

(2) *The syndesmo-chorial* —The membrane comprises the same items as in (1) above, with the exception of the maternal epithelium The gross shape is cotyledonary (or multiplex) and the endometrial relation transitional between non-deciduate and deciduate Placentae of this type are found in ruminants

(3) *The endothelio-chorial* —The membrane comprises the

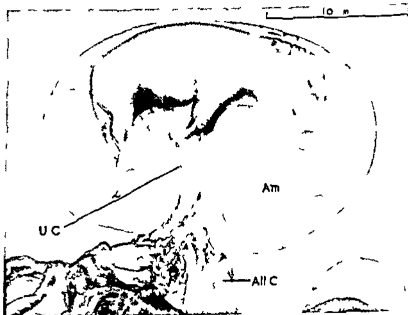


FIG 99b —Pig foetus a litter mate of the one shown in fig 99a with the allanto chorion *All C* dissected away to show the amnion *Am* and umbilical cord *U C*

Figs 103–106 —Diagrammatic sections through various types of placenta (Amoroso)

Fig 103 —Epithelio-chorial placenta of the pig All the layers of the mucosa are preserved and the uterine epithelium is in contact with the chorion

Fig 104 —Syndesmo-chorial placenta of the sheep The uterine epithelium is missing and the chorion is in contact with the maternal connective tissue

Fig 105 —Endothelio chorial placenta of the cat The mucosa is still further reduced and the chorion reaches the endothelium of the maternal blood vessels *P* placental labyrinth *J* junctional zone

Fig 106 —*Labyrinthine* placenta of the guinea pig (Amoroso after Grosser) According to Grosser (1927) this placenta is haemo-chorial i e the endothelium of the maternal blood vessels is broken down and maternal blood comes into direct contact with the chorion According to Mossman (1937) there is probably a further change to haemo endothelial i e maternal blood comes into direct contact with the endothelium of the foetal blood vessels This view criticized earlier by Grosser (1927 131–132) may be regarded as still sub judice *P* placental labyrinth *T* layer of maternal blood spaces lined by syncytiotrophoblast without foetal vessels between them *M* muscularis *A* afferent maternal vessel *E* efferent maternal vessel

the detachment and expulsion of the placenta and the change over from the mature foetal circulation to the post natal one

In the case of the diffuse epithelio chorial placenta for instance there is no very intimate connection between the maternal and foetal structures and the placenta is in one piece Hence separation of the placenta, once it has begun

guinea-pigs, they may, earlier in gestation, have been haemo chorial (fig 106)

The great advance of the above system on previous ones is obvious, but it should be regarded as a right beginning rather than as a final story, for there are many difficulties in connection with its universal application, and considerable research still remains to be done before these difficulties are overcome As Mossman stated in his general summary, "the variations and niceties of adaptations between a female mammal and her intra-uterine young are as infinite and complex as those of any other biological system"

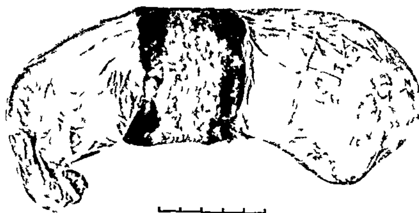


FIG 101 —Dog foetus delivered by Caesarean section at full term showing zonary band of villi on the surface of the chorion Note the *marginal haematome Scale in cm*

After this general summary, one should add that the main points about *the placentae of a large number of eutherian mammals are to be found on* pp 204–32 of Mossman's article One may also note that the physiological exchange of fluids, dissolved substances and gases across the placental membrane has been the subject, during recent years, of numerous experimental investigations The results are a considerable addition to foetal physiology but they will not be summarized in this book, which is not primarily *concerned with such functions of* the foetal circulation, but rather with the rate and amount and other characteristics of the blood flow to the various parts The present writers have not yet made any cineradiographic studies of the flow through the placenta, though such are on their list of agenda Until such records have been obtained and the placental anatomy has been re-studied in the light of the physiological findings derived *from them*, the main interest of this section is in connection with *the third stage of labour*, i e with



FIG 102 —Guinea pig foetus age unknown showing discoid placenta *UW* uterine wall

which are not everywhere equally marked The furrows are caused by the contraction of the circular band of smooth muscle which at this point encircles the two arteries and the vein and the allantoic duct, the vessels have to a large extent lost their surrounding connective tissue The narrowing is shown both in the fig and also in the dimensions recorded by Hauptmann, at 10 4, and 1 cm distance from the skin the cord measured respectively 55 × 12 mm 37 × 14 mm, and 19 × 14 mm The anatomical peculiarities are of importance in relation to the rupture of the cord in this species

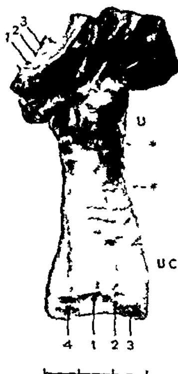


FIG 107 —Horse foetus age unknown Proximal portion of umbilical cord *U C* to show constriction (between asterisks) next to umbilicus *U* 1 left umbilical artery 2 allantoic duct urachus 3 right umbilical artery 4 umbilical vein Scale in cm

(2) *Allantoic and amniotic portions of cord* —In the horse the cord can be regarded as consisting of allantoic and amniotic portions the former extending through the allantoic sac from the allantois chorion to the amnion and the latter through the amniotic cavity from the allantois to the umbilicus The allantoic portion may represent a half to two thirds of the total length of the cord (Williams 1917 1940) Schultze (1896, fig 88) gave a clear picture of the two portions In the cat and the dog the allantoic portion is very short and it is completely absent from ruminants and the pig (Fleming, 1930)

(3) *Length of cord* —Individual and specific variations are found (Fleming) In the dog and the cat the cord length is 2 5 to 5 cm, or about of the body length (Fleming) Williams (1940) said about half the body length In the horse the length of the foetal (intra amniotic) part was given by Gmelin as 70 cm (diameter 2 to 5 cm) i e slightly over half the length (120 cm) of the mature foetus Zietschmann (1924 quoted by Williams) said it was about 100 cm Fleming gave a range of 75 to 100 cm (diameter 8 75 cm) Williams in a series of thirty thoroughbreds found an average of just under 50 cm (about equally divided between amniotic and allantoic portions), the longest cord in the series was 75 cm In four cords Wright (1943) found the allantoic portions 25 35, 20, and 42 5 cm respectively, and the corresponding amniotic portions 1 , 35 50 and 25 cm respectively, i e a total length of 40 to 70 cm A calf 98 cm long had a cord 21 cm long, the calf weighed 30 kg and the placenta 5 5 kg (de Bruin, 1901) Fleming gave a range of 22 5 to 45 cm (about half the foetal length) for this animal and Williams one of 30 to 37 5 cm Minot (1911) said the pig s cord was very short and Jordan's (1919) specimen was but a quarter as long as the foetus Bayer (1900) however, spoke of its great length and Fleming said it sometimes stretched the whole length of the foetus while Williams gave the absolute length as about 25 cm, and claimed that it was relatively the longest cord found among domestic mammals

tends to proceed rapidly to completion If the foetus is so placed that it cannot breathe for itself when the placenta has so begun to separate, the second stage of labour must be rapidly terminated, or the foetus will be in danger of death from asphyxia Where, on the other hand, the placenta is of the cotyledonary syndesmo-chorial type, partial separation is slightly more difficult because of the somewhat more intimate contact between the maternal and foetal structures, and it does not so readily proceed to complete separation because of the subdivision of the placenta into a large number of small scattered masses Placental factors are, therefore, of importance when one considers the birth processes in individual species of mammals (see Chapters V and VIII), on the other hand, they are by no means the only factors involved, so it is unnecessary here to go beyond the two examples already mentioned

This section cannot be concluded without some reference to the innervation and pharmacology of the placental vessels So far as the innervation is concerned, it is a priori unlikely that the placental vessels are innervated if the umbilical ones are not and, as will be seen in section (ii) below, the general finding is that the cord vessels are not innervated An exception, however, is provided by Amoroso's discovery of nerve-bundles within the bovine cord and it will be interesting to learn if his further researches show a carry-over of the innervation to the placental vessels in this species So far as the pharmacology is concerned, the sole references discovered by the present writers are to some work done by Yunoki (quoted by Ueda, 1931, a), who reported that adrenaline was without effect upon the rabbit's placenta, and to a paper by Dawson and Robson (1940), it is, however, possible that other contributions have been overlooked Dawson and Robson perfused placental vessels in situ in nearly full-term cats and bitches Acetylcholine increased the perfusion pressure, adrenaline, except in one experiment, was without effect, posterior pituitary extract caused a sustained rise Here, again, it will be of interest to investigate the bovine placenta, in view of Amoroso's findings about the cord, and to discover if the vessels in this species show any more marked reactions to autonomic drugs

(ii) THE UMBILICAL CORD AND THE UMBILICAL VESSELS

The literature is concerned chiefly with domestic mammals and is not too satisfactory, even in respect of these

(1) *External features of the cord* —Two features only will be mentioned here On the surface of the horse's cord are numerous rough protuberances (fig 108*m*), their sizes vary from that of a millet grain to that of a lentil, and they are formed by local heapings-up of amniotic epithelium (Gmelin, quoted by Hauptmann, 1911) Bigger protuberances are seen on the cord of the hippopotamus (figs 89, 109*e*)

The horse's cord also exhibits a narrowing just before it reaches the edge of the skin of the foetus (fig 107, cf Hauptmann's fig 1) This ring, according to Gmelin, is clear and free of pigmentation and is covered by several layers of epithelium Hauptmann said that its surface is very white, is covered by epithelium similar to that of the skin, and exhibits fine longitudinal furrows

which are not everywhere equally marked The furrows are caused by the contraction of the circular band of smooth muscle which at this point encircles the two arteries and the vein and the allantoic duct the vessels have to a large extent lost their surrounding connective tissue The narrowing is shown both in the fig and also in the dimensions recorded by Hauptmann, at 10 4, and 1 cm distance from the skin the cord measured respectively 35 × 12 mm 37 × 14 mm and 19 × 14 mm The anatomical peculiarities are of importance in relation to the rupture of the cord in this species

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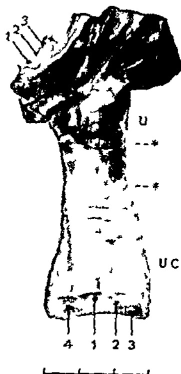


FIG 107—Horse foetu age unknown Proximal portion of umbilical cord *U C* to show constriction (between asterisks) next to umbilicus *U* *1* left umbilical artery allantoic duct urachus *3* right umbilical artery *4* umbilical vein Scale in cm

(3) *Length of cord*—Individual and specific variations are found (Fleming) In the dog and the cat the cord length is 2 5 to 5 cm, or about of the body length (Fleming), Williams (1940) said about half the body length In the horse the length of the foetal (intra amniotic) part was given by Gmelin as 70 cm (diameter 2 to 5 cm) i e slightly over half the length (120 cm) of the mature foetus Zietschmann (1924, quoted by Williams) said it was about 100 cm Fleming gave a range of 75 to 100 cm (diameter 8 75 cm) Williams in a series of thirty thoroughbreds found an average of just under 50 cm (about equally divided between amniotic and allantoic portions), the longest cord in the series was 75 cm In four cords Wright (1943) found the allantoic portions 25 35, 20, and 42 5 cm respectively and the corresponding amniotic portions 17 35 30 and 25 cm respectively, i e a total length of 40 to 70 cm A calf 93 cm long had a cord 21 cm long, the calf weighed 30 kg and the placenta 5 5 kg (de Bruin, 1901) Fleming gave a range of 22 5 to 45 cm (about half the foetal length) for this animal and Williams one of 30 to 37 5 cm Minot (1911) said the pig s cord was very short, and Jordan's (1919) specimen was but a quarter as long as the foetus Bayer (1900) however, spoke of its great length and Fleming said it sometimes stretched the whole length of the foetus, while Williams gave the absolute length as about 25 cm, and claimed that it was relatively the longest cord found among domestic mammals

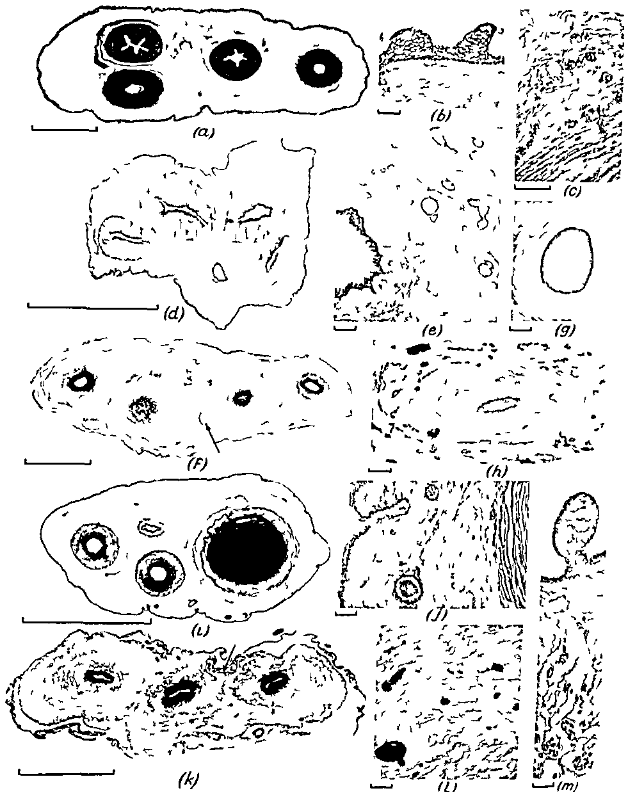


FIG 108 —Scales transverse sections of umbilical cords 5 mm high power views 0 1 mm

a Bovine (*Bos taurus*) foetus *c* 130/*c* 280 days Transverse section of umbilical cord Above from left to right artery allantoic duct artery vein below vein

b High power view of amniotic pustule on surface of same bovine cord

c High power view of peri arterial region of same bovine cord showing several small blood vessels and nerve bundles in the immediate vicinity of an umbilical artery

d Goat (*Capra hircus*) foetus nearly full term Transverse section of umbilical cord Above arteries below vein allantoic duct vein

[*Continued at foot of opposite page*

(4) *Torsion of cord*—The irregular spirals in the amniotic portion of the horse's cord (Gmelin) disappear about 10 cm from the umbilicus (Hauptmann) Williams said that the twist was most marked in the horse, and occurred in both the amniotic and the allantoic sacs He added that the amount of twisting appears to vary with the cord length, and that it is almost prohibited in ruminants by the shortness of the cord[1] In three out of five foals' cords Wright found no twists, there were 4 and 2[1] twists respectively in the other two cords, both portions being affected, two of the cords that had no twists were long ones (67 5 and 70 cm) Jordan found the pig's cord only slightly twisted by comparison with the human one

(5) *Strength of cord*—According to Bayer (1900), tests of the strength of the human cord were begun in 1841 and led later to comparative studies by Kehrer who found that the cord was unable to bear the weight of the foetus in ruminants, etc was usually able to do so in Man, and invariably able to do so in the cat and the dog

(6) *Amount and consistence of cord matrix*—In the horse's cord, according to Gmelin, the arteries and vein are surrounded by a loose connective tissue, in the meshes of which is a varying amount of Wharton's jelly Hauptmann stated that the amniotic sheath is very loosely attached to the vessels by fine fibrous strands and that this intervascular connective tissue becomes more gelatinous towards the umbilical ring Meyer (1914 a) quoted these findings in the horse and added that the matrix is specially great in amount and semi-fluid in character in ruminants such as the sheep and ox Such semi fluidity allows the severed vessels of ruminants (and equidea) to retract as well as contract within the cord while the firmer attachments present in other animals prevent retraction though contraction is possible

(7) *The number of the large blood vessels in the cord* (see figs 108, 109) From the accounts given by Schultze (1896 76–118 passim) and by Popoff (1938) it is obvious that great generic and individual diversity exists Omphalo-mesenteric vessels (pictured by Needham as early as 1667) as well as umbilical ones are present in the cords of some animals (e g the cat and the dog) It would serve no very useful purpose here to list all the available data, but one

[1] This is certainly untrue of the sheep so far as personal experience goes

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Fig 108 continued from foot of previous page]

High power view of part of same goat's cord in vicinity of allantoic duct Note the numerous small blood vessels near the duct

f Arabian camel (*Camelus dromedarius*) foetus age unknown Transverse section of umbilical cord Left to right vein artery allantoic duct (above) remains of yolk sac indicated by arrow (below) artery vein

g High power view of amniotic pustule near surface of same camel cord

h High power view of part of same camel cord showing degenerated remains of yolk sac and small blood vessels nearby

i Pig (*Sus scrofa*) foetus c 95/112–120 days Transverse section of umbilical cord Left to right artery allantoic duct (above) artery (below) vein

j High power view of superficial portion of same pig cord In this genus the main distribution of the smaller blood vessels is to the superficial region of the cord The outer part of an umbilical artery is seen on the right of the section

k Horse (*Equus caballus*) foetus c 140 30/–394 days Transverse section of umbilical cord Left to right vein artery allantoic duct indicated by arrow (above) artery

l High power view of portion of same horse cord showing small blood vessels the distribution of these is much as in the pig cord

m Horse foetus more advanced than last High power view of superficial portion of umbilical cord showing an amniotic pustule and numerous developing smooth muscle fibres

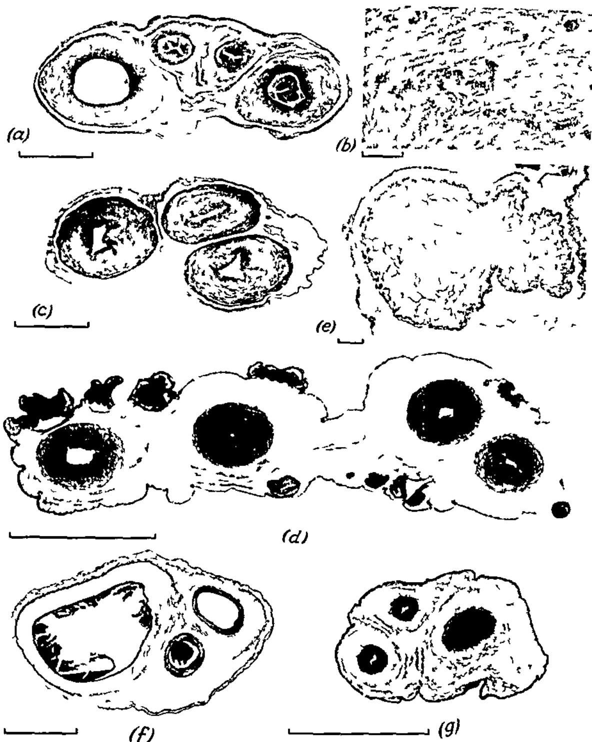


FIG 109 —Scales transverse sections of umbilical cords 5 mm high power views 0 1 mm

a Killer whale (*Pseudorca crassidens*) foetus age unknown Transverse section of umbilical cord Left to right vein artery allantoic duct artery vein

b High power view of portion of same whale cord The small blood vessels are seen in the wall of an umbilical artery i e in an altogether different position from that which they occupy in the cow pig and horse

c African elephant (*Loxodonta africana*) foetus c half term Transverse section of umbilical cord Left to right vein arteries (one above the other) allantoic duct

d Hippopotamus (*Hippopotamus amphibius*) foetus age unknown Transverse section of umbilical cord Left to right vein artery allantoic duct vein artery

e High power view of amniotic pustule from surface of same hippopotamus cord

f Gorilla (*Gorilla gorilla*) foetus full term Transverse section of umbilical cord Left to right vein artery artery

g Colobus (*Colobus occidentalis*) foetus age unknown Transverse section of umbilical cord Left to right, artery artery vein

may with advantage summarize the facts about certain animals which are mentioned fairly often in the subsequent story

In the horse there are two umbilical arteries and, in the more peripheral part of the cord, two venae comites; these veins, however, fuse about 20 to 15 cm from the umbilicus (Hauptmann) so there are only three major blood vessels at the umbilical ring. In the ox there are two umbilical arteries and two venae comites in the cord. The arteries, according to de Bruin, are usually joined by a transverse anastomosis about the middle of the cord, and the veins fuse with one another at the umbilical ring. The goat is very like the sheep. According to Schultze (1896, fig. 93) and Jordan there are two arteries and one vein in the pig's cord; according to Fleming, there are two of each.

(8) *Description of the large vessels of the cord.*—Both the veins and the arteries are remarkable for the thick muscular character of their walls. The histological pictures in different animals have been given by a succession of authors, e.g. Henneberg (1900) and Borodowitsch (1927) described the rat's cord, Bucura (1902) those of the rabbit and dog, Hauptmann that of the horse and Jordan that of the pig; in addition a number of Popoff's pupils published doctorate theses dealing with the cords of various species (summarized by Popoff, 1938). One would be justified in recapitulating these accounts in a monograph on the umbilical cord but scarcely so here. If one is to generalize at all, one may state that there is a tendency for "longitudinal" muscle to lie internal to circular muscle (Bucura, 1902; Popoff, 1938; and others), for the lumina of contracted arteries to be "star-shaped" slits, and for the lumina of contracted veins to be more circular (Popoff, 1938; and others). One must, however, reassert here that histological sections are of themselves inadequate; what one needs in order to understand how the vessels react on post natal severance of their continuity is the result of reconstructions from serial sections, for only in this way can one obtain a proper idea of the internal arrangements, and of the external attachments, of the vascular tube as a whole. Such reconstructions would also decide how far "longitudinal" and "circular" muscle fibres are properly so called. If one strips the "circular" coat of an umbilical vessel it appears to come off in a close spiral. Present accounts of the elastic tissue in the vessels are often conflicting and one would like to see this matter cleared up. No valves are present in the umbilical veins.

(9) *Pharmacology and innervation of the cord vessels.*—In as much as it is easier to do pharmacological tests on large vessels, and human cords are much more readily available than those of large domestic animals, there is practically no literature on the comparative pharmacology of the cord vessels[1]; Waterman (1933, 14) commented on this lack in respect of the umbilical vein. The question as to whether the umbilical vessels are innervated has also been studied mainly in Man, but there are a few references to work on lower animals. Argaud (1922) mentioned a nervous supply but did not give any detailed account of his findings. Ooi (1934) claimed that the cord vessels of the rabbit and the

[1] Professor J. A. Gunn (unpublished observations) found arterial segments taken from various parts of the bovine cord reactive to both sympathetic and parasympathetic stimulants and depressants. The response to adrenaline used in some experiments in concentrations as low as 1 in 20 millions was invariably a contraction.

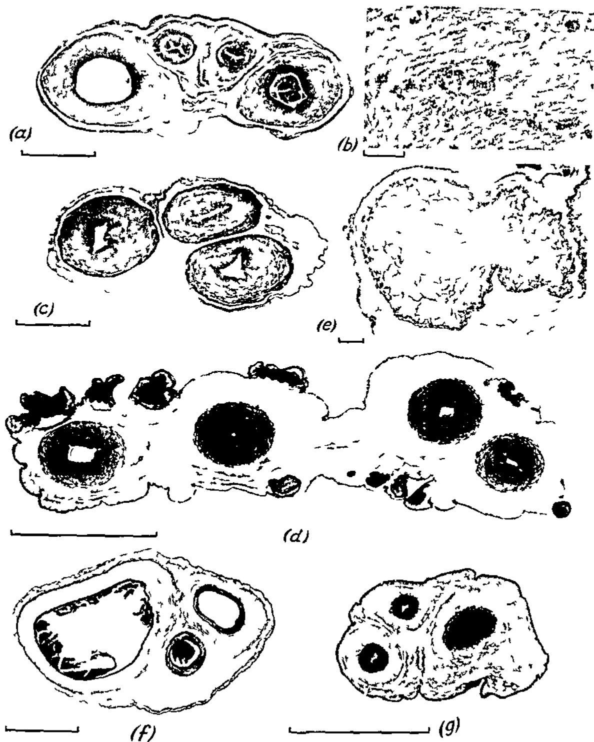


FIG 109 —Scales transverse sections of umbilical cords 5 mm high power views 0 1 mm

a Killer whale (*Pseudorca crassidens*) foetus age unknown Transverse section of umbilical cord Left to right vein artery allantoic duct artery vein

b High power view of portion of same whale cord The small blood vessels are seen in the wall of an umbilical artery i e in an altogether different position from that which they occupy in the cow pig and horse

c African elephant (*Loxodonta africana*) foetus c half term Transverse section of umbilical cord Left to right vein arteries (one above the other) allantoic duct

d Hippopotamus (*Hippopotamus amphibius*) foetus age unknown Transverse section of umbilical cord Left to right vein artery allantoic duct vein artery

e High power view of amniotic pustule from surface of same hippopotamus cord

f Gorilla (*Gorilla gorilla*) foetus full term Transverse section of umbilical cord Left to right vein artery artery

g Colobus (*Colobus occidentalis*) foetus age unknown Transverse section of umbilical cord Left to right artery artery vein

umbilical arteries in its thickness and firmness, the latter was flaccid and collapsed like other veins. Spivack (1943) noted that the umbilical vessels of the guinea pig do not possess an adventitia within the cord, but do have one within the abdomen. The intra-abdominal portions, except in the immediate neighbourhood of the umbilicus, have a rich supply of non-myelinated nerve trunks and nerve fibres which in some areas form larger or smaller meshes. In the African elephant there is a sudden increase in the thickness and contractility of the umbilical arterial wall from about half way between the termination of the aorta and the umbilicus so far as one can judge from the fixed specimen personally examined (fig. 110).

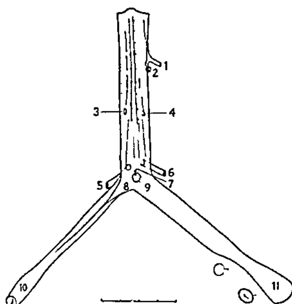


FIG. 110.—African elephant foetus (see fig. 93). Distal part of aorta terminating by giving off the right *10* and left *11* umbilical arteries (cut short just over 1 cm. proximal to internal aspect of umbilicus). Aorta and left umbilical artery opened out. The sudden increase in thickness of the left umbilical arterial wall as the vessel passes towards the umbilicus is shown by the two cross-sections added to the figure. *1* coeliac artery. *2* anterior mesenteric artery. *3* and *4* right and left renal arteries. *5* and *6* right and left external iliac arteries. *7* (black dot) caudal artery. *8* and *9* right and left internal iliac arteries. Scale in cm.

(iii) THE LIVER

In the foetal lamb it is possible to divide the liver into umbilical and portal moieties according to the radiographically observed afferent venous distributions: the anatomical divisions correspond when one includes the sinus intermedius distribution in the umbilical moiety. It would be wrong without further experiment to assume that there is similar agreement in all foetuses, but the findings in the lamb do suggest that, even anatomically, the mature foetal liver can be best described not in relation to its external topography, but in relation to the afferent and efferent venous arrangements. Earlier workers who studied the liver in this way were Rex (1888), Cantlie (1897–8, 1899), and Looten (1908), but all their material (except for one foetal liver examined by Rex) was post-natal and Rex alone looked at the liver in any large series of animals. The anatomical studies of the foetal liver, carried out at the Nuffield Institute, are in consequence novel (1) because of their method of approach and (2) because they have a physiological backing in one species.

The only restriction on the number investigated has been the necessity for examining by the probe, both the afferent and the efferent systems in the same organ: in other words, it has not been possible to dissect unduly small livers. Those that have been studied have shown in their vascular pattern a fundamental similarity which has contrasted markedly with the wide range of generic and specific morphological variation exhibited by the same organs. As will

guinea-pig were innervated by sympathetic fibres, but did not find any carry-over to the placental vessels. Spivack (1943) appears to have gone into the matter much more carefully and critically than her predecessors, and she was unable to find any evidence of a nerve supply to the vessels of the guinea-pig's cord, though the intra-abdominal portions of the same vessels, simultaneously stained, were found to be innervated. Amoroso, however, has found nerve bundles in the bovine cord (fig. 108*c*), and is pursuing the matter farther (personal communication). So the story is not yet complete.

(10) *The attachments of the cord vessels to the umbilical ring.*—Bayer (1900) wrote that in most domestic animals the whole of the umbilical vessels are firmly attached at the umbilical ring, but that in ruminants the vein alone is thus attached, the arteries being so loosely connected that they can move freely in and out of the ring. De Bruin (1901) made a similar statement about the calf, and presumably both his statement and that of Bayer derived from Franck. Meyer (1914, a, b) repeated the note about the looseness of the arterial connections in ruminants, and said that it was otherwise in the pig, cat, rabbit and guinea-pig. Personal experience is in accord with Bayer's statement in so far as the sheep and goat are concerned; it has not yet been possible to check it on bovine material. Williams (1940) said that the umbilical arteries of the horse retract within the abdomen after birth, but that the umbilical vein is fixed to the umbilicus and cannot do so. In view of what Bayer wrote, and of the effects of rupture of the horse's cord described by Hauptmann (1911), one would like confirmation or otherwise of Williams' statement.

(11) *The occurrence of smaller vessels in the cord.*—Goenner (1906) said that Schott (1836) found vasa vasorum, both arterial and venous, in the cord and that the venous ones were specially noticeable in the calf if one slit up an umbilical vena comes and looked for openings on its inner surface. In the pig's cord Jordan (1919) found blood islands and many arterioles, venules, and capillaries. Many of these small vessels, he thought, were vasa vasorum, but others were equally certainly nutrient vessels for the allantoic duct, the ectodermal covering and the general connective tissue. In 1943 Harper demonstrated sections of lambs' cords that contained numerous small vessels. Such vessels have not shown up in the radiographic records of lambs delivered by Caesarean section and injected with thorotrast. Spivack (1943) said that vasa vasorum can occur, exceptionally, in the guinea-pig's cord. Amoroso's series of cords (figs. 108, 109) is much more extensive than any previous one, and he inclines to the view (personal communication) that the distribution of small vessels may be related to placentation types. He wishes, however, to examine certain other cords before publishing any definite conclusions about this and other findings of interest.

(12) *The intra-abdominal portions of the umbilical vessels.*—There is a remarkable dearth of observations about the structure of these vessels, and it would appear that the ovine and human subjects (see Chapters III and IX) are the only ones that have been studied at all thoroughly. *Hofmann (1877)* was struck by the difference between the extra- and intra-abdominal portions of the umbilical vein in the large mammals. The former was very akin to the

is considered in a separate section of this Chapter

The liver of the African elephant foetus (Amoroso, Franklin and Prichard 1941) is arranged very simply in three masses (left central, and right) partially separated by two fissures (figs 111, 112) The papillary and caudate processes and the gall bladder are wanting The posterior vena cava makes contact with the liver near the diaphragmatic foramen only (fig 113) and not, as in most mammals over an appreciable distance, hence there is an absence of accessory hepatic veins uniting with the vena cava caudal to the principal hepatic veins The umbilical vein enters the liver in the middle of its central mass and the line of attachment of the falciform ligament corresponds with a line from the vein's middle to the dextral edge of the termination of the left hepatic vein This line is regarded as a surface demarcation of the two subdivisions of the central mass namely central mass left and central mass right The umbilical vein s offshoots with the small vessel from the sinus intermedius, are distributed to the left mass and the central mass, the portal vein's offshoots are distributed to the right mass The left hepatic vein drains the left mass and the central mass left the middle hepatic vein drains the central mass right, and the right hepatic vein drains the right mass

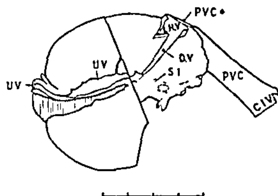


Fig 113—Left lateral view of a central slice of the liver depicted in figs 111 112 To the right of the oblique central line the liver has been cut away farther to a depth of 0 25 cm Hatched area external liver surface *U I* umbilical vein contracted outside liver dilated inside *D I* ductus venosus *S I* sinus intermedius The oval to the right of the sinus is the opening of one of the offshoots of the portal vein *C I I* common iliac vein *P I C* posterior vena cava before and *P I C* after its union with the right and middle hepatic veins *L H I* left hepatic vein Scale in cm

The simple vascular organization exhibited by the elephant liver suggested a general anatomical schema of hepatic constitution underlying the considerable detail presented by a large range of foetal material varying widely both in external configuration and at first sight, in internal venous arrangement Such a schema has stood the test of application to all the livers of other genera examined, despite minor difficulties occasioned by diversity of fissuration It naturally receives scant support from the literature because earlier workers have studied the veins in too few genera (e g Bradley, 1908, Klages, 1931, Matousek 1935) or have studied the adult organ only (Rex, 1888), or have confined attention chiefly to superficial and external hepatic vessels (Flower, 1872, Ruge, 1902–10)

Vascular schema of foetal mammalian liver (figs 114, 115) On the basis of its afferent venous distribution and efferent venous collection, the foetal mammalian liver may be divided anatomically into

(1) An umbilical moiety i e left mass plus central mass plus papillary process and

(2) A portal moiety i e right mass plus caudate process

Papillary and caudate processes are occasionally wanting, and are there-

be described below, this similarity has suggested a schema of the mature foetal liver based on its venous arrangements. Neither the embryonic development of particular blood vessels, nor their ultimate post-natal fate, has been taken into consideration, for the vascular pattern of the liver at term is presumably appropriate to the organism under the conditions obtaining at the time, and can therefore be studied without reference to past or forthcoming anatomical changes.

In the account that follows, references to hepatic "lobes" are avoided (1) because the term "lobe" has hitherto been used somewhat haphazardly, (2) because fissures do not always divide the liver into physiological entities, and (3) because it is frequently difficult to determine how far into the organ a particular portion, superficially demarcated by fissures, extends. No reference is made to a "quadrate lobe," for the term is unnecessary and apt to mislead, and to avoid ambiguity the terms "papillary process" and "caudate process" are substituted for "Spigelian lobe" and "caudate lobe" respectively. The comparative anatomy of the ductus venosus

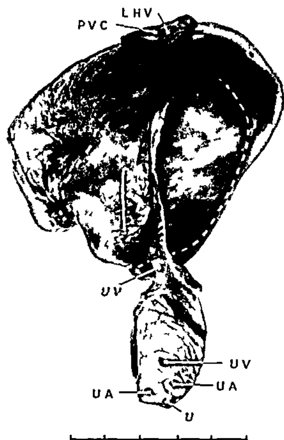


Fig. 111.—*African elephant foetus (see fig. 93).* Ventral view of liver, umbilical vein (*U V*) and umbilicus; the long axis of the abdomen is parallel to the vertical white line. Interrupted lines mark left and right fissures dividing viscus into left, central and right masses. Continuous black line goes from middle of umbilical vein (*U V*) at its entry into the liver along attachment of ligament to right edge of termination of left hepatic vein (*L H V*); it subdivides central mass into central mass left and central mass right. *P V C*, trunk formed by union of posterior vena cava and right and middle hepatic veins. *U A*, umbilical artery. *U*, urachus. Scale in cm.



Fig. 112.—Cranial view of liver depicted in fig. 111. Interrupted black line gives idea of width of posterior vena cava. *Oe*, oesophagus. Other lines and letters as in fig. 111. Scale in cm.

cavally at or about diaphragmatic level as three—left, middle, and right In livers of relatively simple constitution the middle hepatic vein drains the central mass right and the right hepatic vein drains the right mass But in livers absolutely or relatively devoid of deep fissures the main hepatic veins (other than the left) exhibit considerable variations regarding their drainage territories so that it becomes impossible to formulate any description adequately applicable to even the individuals within a single species Fusion of two main hepatic veins before union with the posterior vena cava occurs in several species, and there is considerable variation in the number, size, and aspect of entry into the vena cava of accessory hepatic veins

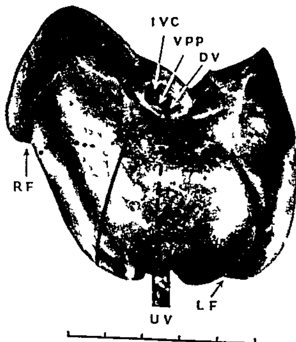


FIG 116.—Cranial view of liver of gorilla foetus (see fig 98) UV umbilical vein RF right fissure LF left fissure IVC inferior vena cava VPP opening of hepatic vein from papillary process DV opening of ductus venosus Interrupted line right edge of mass drained by left hepatic vein Continuous line division between anatomical umbilical and portal masses Dotted line explanation in text Scale in cm

Applicability of schema.—The foetal livers against which the schema has been tested are those of Man, the gorilla lion tiger, dog horse Malayan tapir, calf lamb ordinary goat, Caucasian goat, hog-deer Arabian camel, and pig These form a collection that is very diverse in external morphological configuration and it would be of interest to give the complete details here But lack of space prevents this and the full story must await publication elsewhere For purposes of illustration however one may refer briefly to three livers

The first of these is that of a gorilla foetus (figs 116, 117) There are four fissures (1) a large deep left one, almost subdividing the organ, (2) a smaller but considerable right one (3) a very short, shallow umbilical one (caudal to the umbilical vein) and (4) one that partially delimits the caudate process The caudate and papillary processes are moderate sized with the porta hepatis in between A gall bladder and a ductus venosus are present The inferior vena cava is covered by liver tissue and is much wider at its exit than at its entry In the figures the continuous lines mark the division into anatomical umbilical and portal moieties The left mass lies to the left of the left fissure the central mass left between this fissure and the interrupted line, the central mass right between the interrupted line and the continuous line and the right mass to the right of the continuous line The right mass is partially divided by the right fissure which does not demarcate any particular afferent vascular

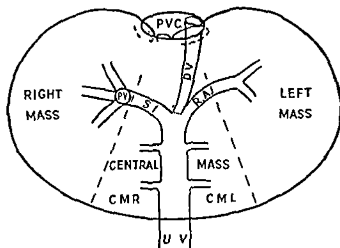


FIG 114 —Schema of the foetal liver in relation to its afferent venous supply *CMR* central mass right *CML* central mass left *UV* umbilical vein *DV* ductus venosus *RA* large last umbilical vein offshoot to the left (ramus angularis of Rex 1888) *SI* sinus intermedius *PV* portal vein *PVC* posterior vena cava

fore omitted from figs 114 and 115

The division between the left and central masses, though marked in some species by a more or less complete fissure, is of minor importance, as it does not separate any major afferent or efferent venous territories On the other hand, the division between the central mass left and the central mass right is important, as separating the territory drained by the left hepatic vein from that drained by other hepatic veins This division line may be defined superficially as that joining the middle of the umbilical vein (at its entry within the umbilical fissure or the homologue thereof) to the dextral edge of the termination of the left hepatic vein In some livers (e g that of *Loxodonta africana*) this line may coincide with the line of attachment of the falciform ligament, in others (e g those of *Ovis aries* and *Sus scrofa*), such coincidence may be partial only, or even wanting The division between the central and the right masses may be marked by a more or less complete fissure, on the other hand, a right fissure may be present (e g in *Gorilla gorilla*), having no relation to hepatic constitution as determined by the venous arrangements Commonly, though not invariably, the line separating the central and right masses coincides with the *mid-line of the gall-bladder, when this organ is present*

The umbilical vein offshoots are distributed to the central mass right, central mass left and left mass, and the sinus intermedius offshoots to the papillary process, when present The opening into a ductus venosus (when present) is an approximate guide to the anatomical division between the umbilical vein and sinus intermedius The portal vein distribution is to the right mass and to the caudate process, if present With regard to the hepatic venous collection, the sole constant feature is the drainage of the left mass and the central mass left by the left hepatic vein Following Rex (1888), one may reckon the standard number of main hepatic veins terminating

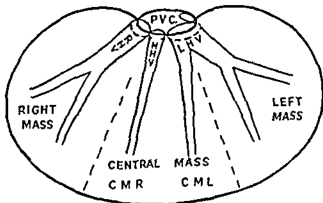


FIG 115 —Schema of the foetal liver in relation to its efferent venous collection *CMR* central mass right *CML* central mass left *RHV* *MHV* *LHV* right middle and left hepatic veins *PVC* posterior vena cava

that of a vein draining mass 4 and caudal to this in succession, are the openings of a vein from mass 5, of a moderately small vein from mass 7 and of one or two small veins from mass 6

The horse liver shows slight intra specific variation It is multifissured (figs 119 120), the umbilical vein lies in a groove on the cranial aspect of the viscus until it enters the organ near the posterior vena cava There is no gall bladder or ductus venosus Seven more or less discrete liver masses are separated by fissures The first fissure extends almost to the vena cava on the cranial aspect and over half-way to it on the caudal aspect, it largely separates mass 1 from mass 2 The second fissure ventrocaudally separates mass 2 from mass 3 (to about the point of entry of the umbilical vein into the liver) and caudally becomes continuous with the ventral part of the first fissure The umbilical vein overlies the second fissure in a groove contributed by masses 2 and 3, an intermediate fissure partly subdivides mass 3 The third fissure partly separates mass 3, ventrocaudally, from mass 4 The fourth fissure extensively separates masses 3 and 4 from mass 5 dorsally approaching closely the posterior vena cava and extending slightly farther on the caudal aspect than the first fissure The fifth fissure separates mass 5 from mass 6 (caudate process) The caudate process is relatively small, the papillary process (mass 7) even smaller, and not overlapping the sinus intermedius The posterior vena cava is covered by masses 7 and 5 save for a dorsal triangular area near the diaphragm The labelling of the liver masses 1–5, in relation to the schema formulated, is rendered feasible only by tracing out the afferent venous supply of these masses—a business made difficult by reason of the

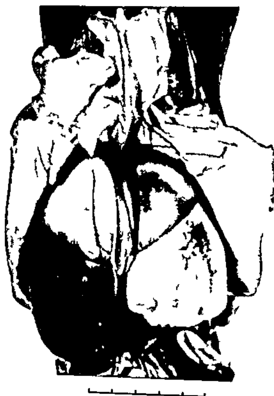


FIG 119—Ventral view of abdomen of a six months horse foetus opened up to show liver and groove for umbilical vein vein itself retracted cranially For division of liver into masses see fig 120 Scale in cm

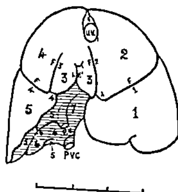


FIG 120—Ventral view of liver of early horse foetus to show masses (numbered 1 to 7) into which liver is divided by fissures *F 1 F* etc fissures 1 2 etc *IF* intermediate fissure *UV* umbilical vein *PV* portal vein *PVC* posterior vena cava Interrupted line mark sides of groove for umbilical vein Scale in cm

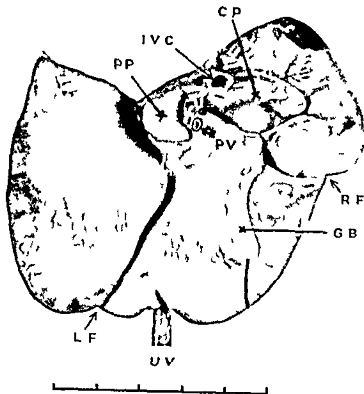


FIG 117 —Caudal view of same liver as shown in fig 116 Continuous line division between anatomical umbilical and portal masses as in fig 116 *P P* papillary process *C P* caudate process *G B* gall bladder *P V* portal vein Rest of lettering as in fig 116 *Scale in cm*

mass The left hepatic vein drains the territory to the left of the interrupted line, in accordance with the schema The next hepatic vein drains the territory between the interrupted and the dotted lines, in *other words, the* hepatic veins other than the left show departures from the schema, as is not uncommon in unfissured or relatively little-fissured organs

The *second* liver *is that of* a lion cub (fig 118) There are four fissures present ventrally, of these the leftmost extends almost to the dorsum *of the organ and separates* mass 1 (left mass) from mass 2 (central mass left), the second extends equally far dorsally on the caudal, less far on the cranial aspect of the viscus, separating mass 2 from mass 3 (central mass right), and lodging the umbilical vein, the third extends to the sinus intermedius on the caudal aspect but not so far as the second fissure on the cranial aspect, separating mass 3 from mass 4 (part of right mass) and lodging the gall-bladder, *the fourth fissure* extends deeply and separates mass 4 from mass 5 (*another part of right mass*) *A fifth fissure,* invisible ventrally, separates mass 5 from mass 6 (part of right mass plus caudate process), finally, a sixth fissure separates mass 7 (papillary process) almost wholly from the rest of the organ The anatomical umbilical moiety comprises masses 1, 2, 3, and 7, the anatomical portal moiety comprises masses 4, 5, and 6 The posterior vena cava is uncovered along the caudal aspect of mass 6 only The left hepatic vein drains the left mass and the central mass left, and the middle hepatic vein the central mass right, as in the schema To the right of the opening of the middle vein is

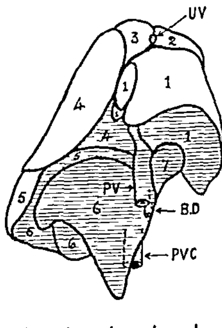


FIG 118 —Ventral view *of liver of* newborn lion cub (see fig 97) Liver masses numbered from 1 to 7 *U V* umbilical vein *P V* portal vein *B D* bile duct *P V C* posterior vena cava Scale in cm

moiety The left hepatic vein drains the left mass and central mass left, as anticipated from the schema, the remaining hepatic drainage exhibits departures from the schema in consequence of the excessive fissuration Mass 3 drains into the middle hepatic vein mass 4 into this vein and a small accessory one, mass 5 into the right hepatic vein and another caudal thereto About the level of this last vein opens a vein from mass 7 and, most caudally of all a vein from mass 6

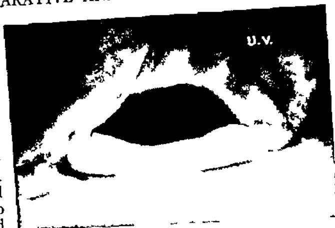


Fig 121*d*

(iv) THE DUCTUS VENOSUS



Fig 121*e*

Colin (1873) found no trace of the ductus venosus in "solipedes but held that it must be present in them in the earliest days of embryonic life as it develops from the omphalo mesenteric vein According to Bradley (1908) it is apparent at 22 days, i e at the 8 mm embryo stage, in the pig Klages (1931) said that it begins to retrogress very early in the pig and the horse but functions right up to birth in carnivores and ruminants Exceptionally, it may be absent from these last Klages himself noted such a case in a lamb and he referred to Franck s findings in the calf (Franck 1875) Van Gelderen (1933) likewise acknowledged the possibility of exceptions to

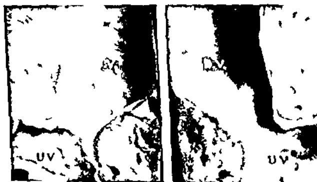


Fig 121*f*



FIG 121*a*

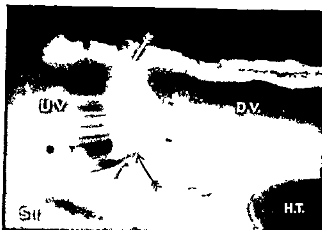


FIG 121*b*



FIG 121*c*

FIG 121 —*a* Bovine foetus over 7½ months Two views of slightly lipped opening from umbilical vein into ductus venosus

b Bovine foetus nearly full term View of right half of junctional region of umbilical vein *U V* ductus venosus *D V* and sinus intermedius *S I* to show prominent smooth muscle sphincter (between arrows) at beginning of ductus venosus (cf fig 122) Top of figure cranial bottom caudal left ventral right dorsal *H T* hepatic tissue Scale 5 mm

c Bovine foetus nearly full term Junction of ductus venosus (above) and umbilical vein (below) divided in the long axis of the ductus to show ridge formed by smooth muscle sphincter at beginning of channel Scale 1 cm

d Bovine foetus nearly full term To show partially contracted sphincter of ductus venosus *U V* umbilical vein Scale in mm

e Bovine foetus nearly full term To show iris like appearance of nearly fully contracted sphincter at *beginning of ductus venosus U V umbilical vein Scale in mm*

f Calf just born To show narrowing produced by sphincter at beginning of ductus venosus *D V* *U V* umbilical vein Scale 1 cm

absence of a ductus venosus and by an atypical spacing of venous offshoots imposed by the liver fissuration Such exploration of veins suggests that mass 1 = left mass, mass 2 = central mass left, mass 3 = central mass right, and masses 4 and 5 = right mass Masses 1, 2, 3, and 7 therefore constitute the anatomical umbilical moiety, masses 4, 5, and 6 the anatomical portal

(8) *Horse* —In a foetus of 140 days the presence of a ductus was uncertain, from a six months' old foetus the channel was definitely absent

(9) *Malayan tapir* — In the single foetus examined no ductus was observed

(10) *Calf* —The liver was removed from a calf that died during birth and shortly afterwards contrast medium was injected under screen observation, into the umbilical vein The filled ductus presented an appearance very similar, though on a larger scale, to that presented by the ductus of the lamb The calf's ductus is provided with a sphincter at its beginning (figs 121 122) and unites with the posterior vena cava either by a discrete orifice sinistral to that of the left hepatic vein, or else by an opening common to it and to this vein Occasionally, both in the foetal and in the post natal animal a vessel or vessels may be encountered entering (or leaving) the ductus despite Klages (1931) statement, "Aus dem Ductus venosus geht kein Gefass hervor" Both Klages and Matousek (1935) figured and described the channel in this species After birth, the ductus may for some time remain pervious except at its beginning



FIG 123 —Goat foetus 136 147 days Part of frame from direct cineradiographic record of an umbilical vein injection To show relative calibre of ductus venosus and slight notching at its beginning (cf fig 83) Scale = cm on radiographic record

(11) *Ordinary goat* —A direct cineradiographic record was made during an injection into one of the umbilical venae comites of the cord The foetus was said to be 136 days old and it weighed 2 kg It had been delivered by Caesarean section, the cord was undivided and pulmonary respiration was prevented by a nose bag The umbilical stream was probably narrowed through contraction of the injected vein after an unsuccessful first attempt to get a needle into its lumen The ductus (fig 123) appeared to be relatively larger than in the lamb its general appearance however, was very similar and in some frames there was some notching at the beginning of the channel, i e there was, presumably a sphincter mechanism at that point

(12) *Caucasian goat* —In the single foetus examined the ductus venosus was blind at its umbilical vein extremity not far from which a single small vessel

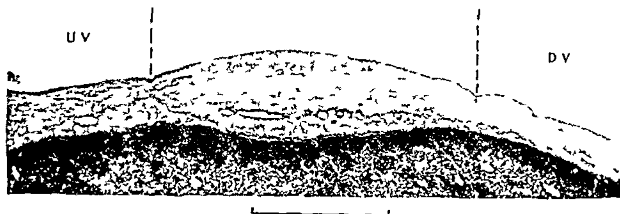


FIG 122—Bovine foetus nearly full term Longitudinal section through junctional region of umbilical vein *U V* and ductus venosus *D V* to show smooth muscle sphincter (fig 121*b* is a macroscopic view of the other half of the specimen) The sphincter extends superficially between the interrupted lines Immediately below it is a paler layer of oedema and between this and the darkly stained liver tissue is a layer with numerous blood vessels Scale 1 mm

his general statement, which was to the effect that, so far as is known, the ductus venosus occurs only in rodents, carnivores, ruminants, and primates

In view of the relative paucity of the literature, the following personal observations may be of interest

(1) *Gorilla*—The foetus studied showed a ductus lipped at its beginning (i e having a sphincter) and broadening out as it pursued an almost straight course to its termination, dorsal to and between the left and middle hepatic veins

(2) *Lion*—In each of two lion cubs examined, the ductus venosus was wide, with a suggestion of lipping at its beginning In one specimen, just within the lip, appeared an offshoot to the papillary process In both specimens the caval opening of the ductus was discrete and lay dorso-sinistral to that of the leftmost hepatic vein

(3) *Tiger*—A very short, wide ductus was found, with a caval opening disposed similarly to those in the lion cubs

(4) *Dog*—In the specimens examined, the ductus venosus, the hepatic veins from the anatomical umbilical moiety and in hepatic vein from the right mass opened, about diaphragmatic level, into a sinus, which then turned to the right to unite with the posterior vena cava

(5) *Brown bear*—The specimen of liver available was in too poor a state of preservation to permit of any tracing of its vessels, there appeared, however, to be a ductus uniting with the posterior vena cava

(6) *False killer-whale*—The hepatic veins were the only vessels that could be followed at all well in the sole specimen available, and no ductus venosus was observed

(7) *African elephant*—In the half-term foetus examined, a ductus venosus was present (fig 113) and it was provided with a sphincter at its beginning (Amoroso, Franklin and Prichard, 1941) The ductus pursued a straight course to enter the dextral aspect of the left hepatic vein It is not known whether the channel persists till birth in this species

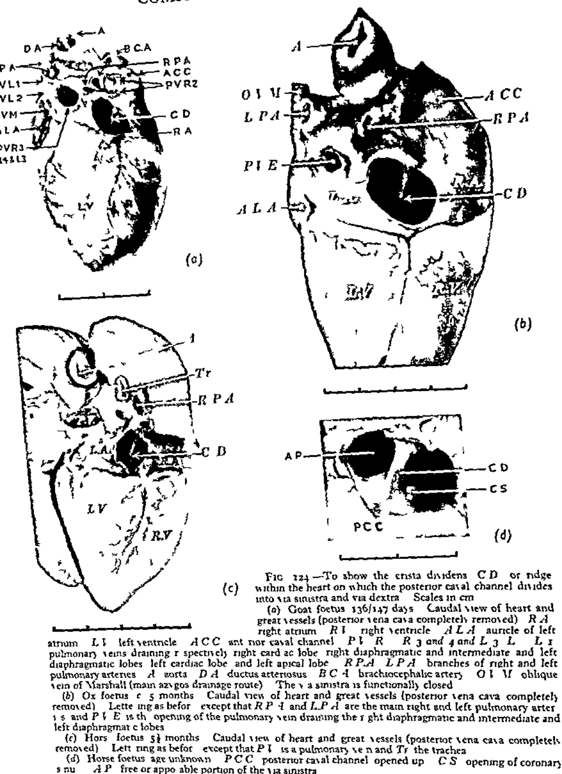


FIG 124—To show the crista dividens C D or ridge within the heart on which the posterior caval channel divides into via sinistra and via dextra Scales in cm

(a) Goat foetus 136/147 days Caudal view of heart and great vessels (posterior vena cava completely removed) R A right atrium R V right ventricle A L A auricle of left atrium L V left ventricle A C C anterior caval channel P V R R 3 and 4 and L 3 L L 1 pulmonary veins draining respectively right cardiac lobe right diaphragmatic and intermediate and left diaphragmatic lobes left cardiac lobe and left apical lobe R P A L P A branches of right and left pulmonary arteries A aorta D A ductus arteriosus B C A brachiocephalic artery O V M oblique vein of Marshall (main azygos drainage route) The via sinistra is functionally closed

(b) Ox foetus c 5 months Caudal view of heart and great vessels (posterior vena cava completely removed) Lettering as before except that R P A and L P A are the main right and left pulmonary arteries and P V E is the opening of the pulmonary vein draining the right diaphragmatic and intermediate and left diaphragmatic lobes

(c) Horse foetus 5½ months Caudal view of heart and great vessels (posterior vena cava completely removed) Lettering as before except that P V is a pulmonary vein and Tr the trachea

(d) Horse foetus age unknown P C C posterior caval channel opened up C S opening of coronary sinus A P free or apposable portion of the via sinistra

entered (or left) it There was a combined caval entry of the ductus and left hepatic vein, the ductus opening being to the left of the hepatic vein opening

(13) *Hog-deer* —The first specimen examined showed a large ductus venosus, unique in personal experience by reason of its union with the vena cava well caudal to the main hepatic veins In a second specimen (5 days post partum) the entry from the umbilical vein into the ductus was closed and showed a slightly elevated surround, otherwise the ductus was still patent and united with the left hepatic vein just before their joint union with the posterior vena cava

(14) *Arabian camel* —The animal examined was a young foetus, about 1 kg in weight (Needham, 1931, quotes from Przibram a birth weight of 80 kg for the species) A large ductus venosus was present, it and the combined left and middle hepatic veins united jointly with the posterior vena cava

(15) *Pig* —In the youngest pig foetus examined a ductus was but very doubtfully present, from two older foetuses it was definitely absent

(v) THE POSTERIOR CAVAL CHANNEL AND ITS TERMINAL BIFURCATION

In the majority of foetuses examined, the posterior caval channel inclines to the left, while the pre-terminal portion of the anterior caval channel (see section ix below) inclines to the right

The crista dividens, which is of such importance to the circulatory story in the lamb (Chapters III and IV), was noted by Ziegenspeck in the guinea-pig during the course of his first researches (Ziegenspeck, 1884) It has been found in all the foetuses personally examined, and it is still present after the whole of the posterior/inferior vena cava has been removed Views of it from the caudal and other aspects are given in fig 124

In mature foetuses, the via dextra at first sight appears to be about equal in calibre to the via sinistra But its calibre is functionally reduced by the flows through the anterior caval channel and the coronary sinus, and this latter in many animals includes a large part of the azygos venous return

(vi) THE VIA SINISTRA AND ITS PARS LIBERA

References to earlier work, and an account of his own findings, were given by Mosca (1914)

The foetuses and immediately post-natal animals, on the examination of which this section is mainly based, are much the same as those on which section (viii) below is mainly based

The lie of the via sinistra, in relation to the body as a whole, may be affected by

(1) The lie of the heart in relation to the dorso-sternal mid-line (see section x below), and

(2) The fact that in some foetuses the apex is more caudal, in relation to the rest of the heart, than in others

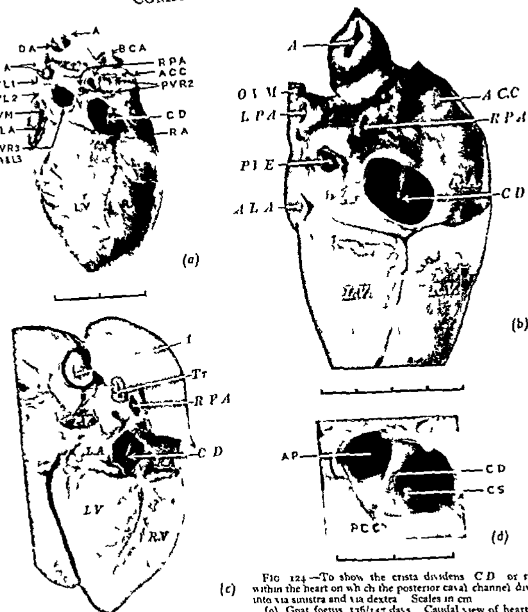


FIG 124.—To show the crista dividens C D or ridge within the heart on which the posterior caval channel divides into via sinistra and via dextra. Scales in cm.

(a) Goat foetus 136/147 days. Caudal view of heart and great vessels (posterior vena cava completely removed). R A right atrium, R V right ventricle, A L A auricle of left atrium, L V left ventricle, A C C anterior caval channel, P V R 1, R 2, R 3 and 4 and L 3, L 2, L 1 pulmonary veins draining respectively right cardiac lobe, right diaphragmatic and intermediate and left diaphragmatic lobes, left cardiac lobe and left apical lobe. R P A, L P A branches of right and left pulmonary arteries. A aorta, D A ductus arteriosus, B C A brachiocephalic artery, O V M oblique vein of Marshall (main azygos drainage route). The via sinistra is functionally closed.

(b) Ox foetus c 5 months. Caudal view of heart and great vessels (posterior vena cava completely removed). Lettering as before except that R P A and L P A are the main right and left pulmonary arteries and P V E is the opening of the pulmonary vein draining the right diaphragmatic and intermediate and left diaphragmatic lobes.

(c) Horse foetus 5½ months. Caudal view of heart and great vessels (posterior vena cava completely removed). Lettering as before except that P V is a pulmonary vein and Tr the trachea.

(d) Horse foetus age unknown. P C C posterior caval channel opened up. C S opening of coronary sinus. A P free or apposable portion of the via sinistra.

The course of the via sinistra, in relation to the heart itself, may also vary as follows

(3) Viewed from the sternal aspect, it may be relatively straight, or it may curve slightly, or it may bend round so far that the blood stream leaves it almost at right angles to its original course within the posterior/inferior caval channel

(4) Viewed from the left side, it may pass due cranially, or incline somewhat sternally or dorsally from that line

In addition to the above possible variations of direction, the via sinistra may remain of approximately the same calibre throughout its course, or it may gradually narrow, or it may narrow in its first part and thereafter remain fairly constant, or it may narrow and then open out and finally be reduced again in calibre

Obviously, the number of variables is very great, and at first glance it would appear that the protean character of the via sinistra is shared by its pars libera also But one is able at the outset to introduce a simplifying concept, namely, that the pars libera is of a fairly uniform type throughout the primates and carnivores examined, and that it departs from this type only in the cetacea, proboscidea, perissodactyla and artiodactyla examined, of its form in other orders of mammals personal experience is lacking

The primate-carnivore type is diagrammatically pictured in fig 156, which is drawn from a human specimen In such a pars libera one can distinguish free and attached borders, and sternal and dorsal cornua To the right of the pars libera (i e behind it in the figure) is the crista dividens This simple type of pars libera can vary in the following ways

(1) In its dorso-sternal width

(2) In its caudo-cranial length

(3) In its inter-cornual distance

(4) One or other cornu may be more cranial, or both may be at the same level

(5) In the slackness or tenseness of the membrane

(6) In the degree of muscularity of the membrane

(7) *In the presence or absence of fenestration of the membrane*, such fenestration is, actually, more common in the other orders examined

(8) In the distance of the crista dividens from the free and attached borders, both in the caudo-cranial plane and also laterally If the middle of the crista is cranial to the middle of the free border, one can see through from the left into the right atrium, or on to the pars libera viae dextrae ("Eustachian valve")

(9) The terminal parts of the cornua may, exceptionally, be mere ridges on the endocardium, in which case the terminations of the free border are not the same as those of the cornua, but are caudal to these latter

(10) The pars firma and the pars libera can contribute varying amounts to the total circumference of the opening of the via sinistra into the left atrium

It is clear, from the above list, that even the primates and carnivores can show considerable variations, in respect of the pars libera viae sinistrae, within the general type form *Even so, the mere existence of such a general type is an enormous simplification when one is investigating a large number of specimens*

In the gorilla foetus examined (full-term or practically so), the pars libera is a

simple, slack flap and the middle of its free border lies some distance caudal to the crista dividens (fig 125) so it would have had to contract up during birth to ensure the occlusion of the via sinistra it appears to be sufficiently muscular to have done this Details about certain other primates are available elsewhere (Franklin Amoroso, Barclay and Prichard 1942 34) but in general the specimens of this order require no special comment

Nor, on the whole, do the carnivores examined with the exception of the brown bear foetus in which the via sinistra passes almost due left and very little cranially The others show the usual range of variations in the relation of the pars libera to the crista dividens the relative lie of the cornua and so on In each of two 10 days' post natal puppies the pars libera occludes the via sinistra but anatomical closure has not set in, in a two months post natal fox cub it has done so

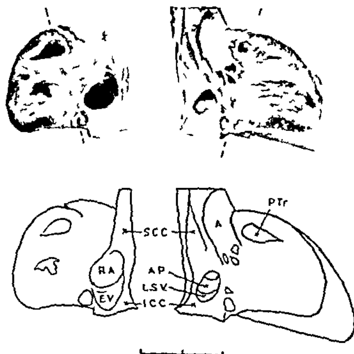


FIG 125—Gorilla foetus (see fig 98) Views revealed by cut through heart etc at first (up to interrupted lines) in "long axis of inferior vena cava and thereafter at an angle to this (see interrupted line in fig 129 e) *SCC ICC* superior and inferior caval channels *EV* Eustachian valve *RA* right atrium *LSV* remains of left sinus valve *AP* free or apposable portion of via sinistra *A* aorta partially divided at level of aortic valve *PTr* pulmonary trunk Scale in cm

When one passes to the representatives of the other orders examined, one finds much more to say, and one realizes the aptness of the epithet "tubular" that was applied to the via sinistra by Wolff (1776) In the African elephant foetus (age about half term) the pars libera is still fairly simple but is relatively long from attached border to cornua (fig 126), the dorsal cornu is more cranial than the sternal one, and the free border contributes about half the circumference of the opening of the via sinistra into the left atrium From the free border a number of "guy ropes" (cf Chapter III section v) pass to the atrial wall In the Arabian camel foetus, a far from mature specimen, the pars libera is pigmented black and shows up clearly against the light coloured parts around it It contributes about half the circumference of the opening into the atrium Like the corresponding structure in the elephant it is not generally different from the primate carnivore type In the deer goat, pig, and sheep foetuses, however, the pars libera commonly reaches an appreciable distance cranial to the crista dividens and contributes over half the circumference of the

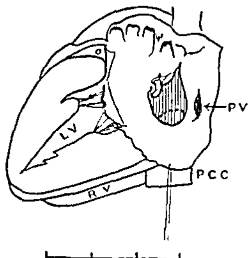


FIG 126 —African elephant foetus (see fig 93) View of heart from left with pulmonary sinus and left atrium divided and reflected caudally and part of left ventricle removed To show free or apposable portion (vertical hatching) of via sinistra Interrupted line approximate level of crista dividens *P V* opening of pulmonary veins draining right apical and cardiac lobes *P C C* posterior caval channel *R V L V* right and left ventricles Scale in cm

opening into the atrium (in the deer about three-fifths, in the goat about three-fourths, and in the pig and sheep on occasion as much as six-sevenths, though individual variations are possible in each genus) These two points ensure a very obvious tubular character to the via sinistra

A still more complex pars libera is found in the foetal calf (fig 127) The tubular via sinistra in this genus is very long and may reach right across the left atrium The pars firma reaches for some distance on the cranial side, but even on this side the terminal portion is contributed by the pars libera alone Often, though not invariably, the tube has no single, comparatively wide opening to mark its ending, but exhibits in its distal half or so a large number of fenestrations The appearance in some specimens (see, e g, fig 127) justifies Kilian's (1826, legend of his fig 5) earlier description of the tube, for he said that it was like the finger of a glove, a better simile, in view of the fenestrations, would be a worn-out finger stall One cannot give, as one can in the case of the lamb, the stages in which this remarkable pars libera is apposed to occlude the via sinistra, but the process is effectively carried to completion, as post-natal specimens show

More free-lying still is the pars libera in the tapir, hippopotamus, and horse In all these animals the via sinistra passes to the left and somewhat dorsally, and also bends round so that its final course is at an appreciable angle to that of the posterior caval channel The bending is least in the tapir, in the hippopotamus and horse it is to nearly a right-angle In the tapir foetus the pars libera lies completely free before it ends by a single wide opening into the left atrium This opening has a sort of lid that is free to close it, the "hinge," so to speak, being on the medial side and the "lid" being directed cranially in the open position Whether the via sinistra is like this in all tapir foetuses one cannot say, nor is the closing of the lid to be regarded as the only apposition undergone by the pars libera after birth In the hippopotamus foetus (so far as one can judge from specimens either inadequately fixed, or else fixed so that the blood is over-hard), the via sinistra is attached over part of the dorsal wall of the left atrium, and the pars libera to the left of this may have "guy-ropes" attaching it to the dorsal and lateral walls of the atrium The pars libera is fenestrated, and the fenestrations in the main face sternally The above description, based on three badly fixed specimens, could doubtless be bettered if one had a single carefully fixed foetus to dissect In the horse foetus the bulk of the via sinistra is provided by its free-lying pars libera, which may be fenestrated to the extreme in its terminal

portion, forming thereby a structure that is arresting in virtue of its sheer beauty (fig 128)

As noted in Chapter III, "via sinistra" and "pars libera viae sinistrae" are terms that have been substituted by the present writers for "foramen ovale" (in one of its connotations) and for "the valve of the foramen ovale"

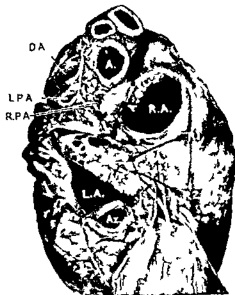


FIG 127

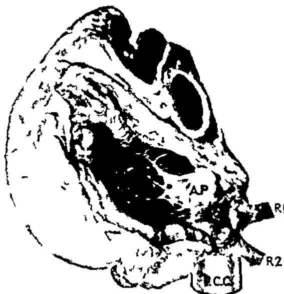


FIG 128

FIG 127 —Calf stillborn Dorsal view of the heart etc Before the specimen was fixed the posterior caval channel *PCC* was slit open the dorsal wall of the left atrium etc was removed and the via sinistra packed in the fully open position Part of the cut left atrial wall is retracted cranially thereby compressing the ductus arteriosus *DA* and the right and left pulmonary arteries *RPA* *LPA* *ACC* the terminal portion of the anterior caval channel *RA* *LA* right and left atria *Az* continuation of oblique vein of Marshall (main azygos drainage route) *A* aorta *AP* the free or apposable portion of the via sinistra The white arrows indicate the course of the posterior caval stream and its left and right terminal divisions The two black arrows *R 1* *R 2* indicate the approximate directions of the blood streams in the pulmonary veins from the right apical and cardiac lobes respectively the entries of these veins were in intimate relation to *AP* the veins themselves were almost completely removed by the preliminary dissection of the specimen and only small portions of the sternal walls of their entries are visible Scale in cm

FIG 128 —Horse foetus full term Dorsal view of part of the heart etc The specimen is incomplete in the right upper part of the figure Before it was fixed the dorsal wall of the left atrium etc was removed and the via sinistra packed in the fully open position To show in its entirety the free or apposable portion *AP* of the via sinistra the photograph was taken from a point somewhat to the left and dorsally *PCC* posterior caval channel *R 1* *R* pulmonary veins (packed with cotton wool) from the right apical and cardiac lobes respectively entering the left atrium in intimate relation to *AP* Scale in cm.

respectively There is no need to repeat here the reasons for changing the first term With regard to the second term there are anatomical and functional reasons for the change Though the primate-carnivore type of pars libera is not unlike the unicuspid parietal valve found here and there in veins some of the others just described are obviously very unlike any of the ordinary valves present in the cardiovascular system Functionally, these ordinary valves

close when the pressure on their distal side rises above that on their proximal side; in the case of the valves of the heart, pulmonary trunk and aorta, such closure is constantly occurring; in the case of the venous valves it takes place much less frequently and at irregular intervals, but it presumably occurs fairly often. With regard, however, to the pars libera viae sinistrae, the only retrograde movement that it is definitely known to make is that which effects the functional closure of the via sinistra after birth. It is conceivable that a powerful respiratory effort in utero might effect a transient closure in the same way, but such efforts must be infrequent during the latter half of gestation, when the inhibitory influence of the higher nervous centres is dominant, and in the earlier part of gestation the pars libera has not reached its full development. So it would seem that the structure is destined mainly, if not exclusively, for the closure of the via sinistra just after birth. Readers may judge for themselves whether or not it is right to give the same name of "valve" to a structure that functions perhaps once only, and to structures that continue to function throughout life.

(vii) THE VIA DEXTRA

Direct radiographic evidence has shown that, in intact sheep and goat foetuses towards term, a minor part of the posterior caval stream goes to the right. As a result of experiments involving opening of the thorax, Windle and Becker (1940) concluded that all, or nearly all, of the posterior caval stream passes to the left side in cat and guinea-pig foetuses during the last third of gestation. There is, therefore, *physiological* justification for speaking of a via dextra in the lamb and the kid, and perhaps also in the foetal kitten and guinea-pig. From the *anatomical* evidence so far accumulated, it would appear that some part of the posterior caval blood must pass to the right in *all* mature foetuses; the crista dividens is there to divide the stream and there is a pathway to the right.

The via dextra is a comparatively short channel; in all animals the free border of the crista interveniens may be regarded as its termination on the cranial aspect; in animals that have a Eustachian valve, the free border of this latter may be regarded as a second limit of the channel, i.e. the valve is the pars libera viae dextrae. In giving this name to the valve, one realizes that the structure in question is not developmentally comparable to the pars libera viae sinistrae,[1] and also that it may persist for a long time after birth without undergoing changes like those undergone by the pars libera viae sinistrae. On the other hand, as Ziegenspeck and others before him pointed out, the two structures are very comparable in their relations to the right and left terminal divisions respectively of the posterior caval channel. One cannot yet say, with certainty and with completeness, what are the functions of the Eustachian valve, but in the mature foetus, while the umbilical venous flow continues in full strength, only posterior caval blood, one imagines, can be in contact with the valve on its caval aspect. The same must be true of the pars libera viae

[1] In foetuses of *Gorilla gorilla* (fig. 125) and *Leontocebus rosalia* examined, as also in an adult *Hystrix longicauda*, both the Eustachian valve and also its embryological counterpart, i.e. remains of the left sinus valve, are present (cf. Weber, 1927, I, 318).

sinistrae, so there is at least this degree of functional similarity between the two structures during the latter part of gestation

Actually, most of the foetuses examined by the present writers have had no Eustachian valve and the via dextra has consisted of a pars firma alone The point is of some interest for Sabatier based his original hypothesis of the course of the foetal blood flow upon a supposed function of this valve For this reason and also because conjecture is very different from objective evidence, it is quite wrong to refer to the radiographic findings in the lamb and the kid as confirming Sabatier s hypothesis, in neither animal is there a pars libera viae dextrae

(viii) THE LOBATION OF THE LUNGS THE PULMONARY VEINS AND THE RELATIONS OF THEIR OPENINGS TO THE VIA SINISTRA

The lobation of the lungs has been examined in representatives of primates carnivora cetacea, lagomorpha proboscidea, perissodactyla and artiodactyla Most of the material examined has been foetal, but some has been post natal and a very small fraction adult (Franklin, Amoroso, Barclay and Prichard, 1942)

The typical right lung has four lobes, and the typical left lung three lobes On each side as in the lamb, there are apical, cardiac, and diaphragmatic lobes, on the right, in addition there is an intermediate, or mediastinal or azygos lobe The separation of the apical and cardiac lobes is usually better marked on the right side than on the left side

One need not list and explain here all the variations from the typical lobation which have been encountered but one may perhaps insert a few notes

In the gorilla foetus examined (fig 129) there are four lobes on the right side and they are well, but not completely, separated The fourth is presumably a lobus intermedius but it lies entirely dorsal to the short thoracic inferior vena cava The left lung is completely divided into two, the more cranial part corresponding to the apical and cardiac lobes of other animals In the adult gorilla examined the lungs are in general similar, but the right apical and cardiac lobes are completely separate while the lobus intermedius is relatively small and less discrete On the left side a large apical and a small cardiac lobe are partially separated by an external fissure The specimen of *Colobus occidentalis* has nine lobes on the right and four on the left side, but these can without much difficulty be grouped to correspond with the typical lobation The baboons have four completely separate lobes on the right side the other primates examined are somewhat similar but vary in the degree of separation of lobes especially in respect of the left apical and cardiac ones

In all the carnivores examined there is a complete, or almost complete, separation of the four lobes on the right side this may be typical of the order as a whole On the left side there are three lobes the diaphragmatic one almost invariably separate the other two varying in their degree of fusion but being always to some extent distinguishable

In the single whale foetus studied the lungs resemble in their arrangement those of the horse (see below) but there is no distinct lobus intermedius

FIG 129 —Gorilla foetus ? full term (see fig 98) Right (*a*) and left (*b*) lateral sternal (*c*) and dorsal (*d*) and caudal (*e*) views of thoracic viscera *R 1 R R 3 R 4* right apical cardiac diaphragmatic and intermediate lobes *L 1 L* fused left apical and cardiac lobes *L 3* left diaphragmatic lobe *R A L A* right and left atria Between them in the caudal view *e* is the inferior caval channel with crista dividens apposable portion of via sinistra and Eustachian valve just discernible *I C C* inferior caval channel *R V L V* right and left ventricles *A* aorta *Tr* trachea *O* oesophagus *Th* thymus etc Scale in cm (The interrupted line in fig 129 *e* gives the direction of the cut which produced the views shown in fig 125)

In the rabbit all seven lobes are found, but they vary in their degrees of separation

In the African elephant foetus (Amoroso, Franklin and Prichard, 1941) the seven lobes can be distinguished with some difficulty and with some residual uncertainty, lobulation being more marked a feature than lobation

In the horse (fig 130) the lungs are not lobated in the usual way, following

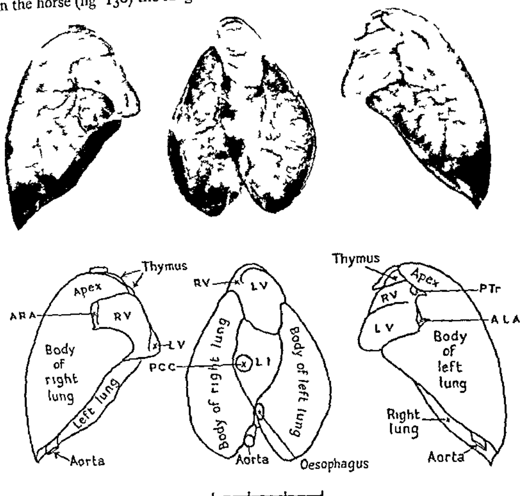


FIG 130—Horse foetus *c* 100 *c* 308 days Right lateral caudal and left lateral views of exsected thoracic viscera *PCC* posterior caval channel *ARA* *ALA* auricles of right and left atria *RV* *LV* right and left ventricles *PTr* pulmonary trunk *LI* lobus intermedius of right lung Scale in cm

Sisson (1940) one can say that on each side there is an apical portion and a body and on the right side, in addition, a lobus intermedius The tapir foetus is similar, at least in respect of the left lung (the right one had been removed before the specimen was received)

The bovine lungs and the goat s lungs are arranged very much as in the lamb in the hog deer the demarcation between right diaphragmatic and intermediate lobes is not easily discovered and the left apical and cardiac lobes

are fused In all these animals, as in the lamb, *the right apical lobe overlaps the mid-line of the body* Such overlap is not apparent in the pig, which in other respects is not very dissimilar to the lamb *The camel's lungs present a picture that is in general similar to the equine, but there is some overlap by the right apical lobe The hippopotamus resembles the horse*

In general, then, on macroscopic appearances and without reference to embryology, *one can divide all right lungs into four lobes or equivalent masses, the fourth lobe being the lobus intermedius, and one can divide all left lungs*

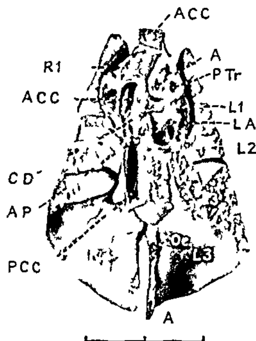


FIG 131 —*Pig foetus c 90/112–119 days* View of dorsal half of thoracic viscera divided by a side to side cut in the long axis *of the posterior caval channel P C C R 1 R 2 R 3 R 4 right apical cardiac* diaphragmatic and intermediate lobes *L 1 L 2 L 3* left apical cardiac and diaphragmatic lobes *A C C* anterior caval channel *C D* crista dividens *A P* free or apposable portion (divided by the cut) of the via sinistra *L A* left atrium *1* aorta *P Tr* pulmonary trunk *Oe* oesophagus Scale in cm

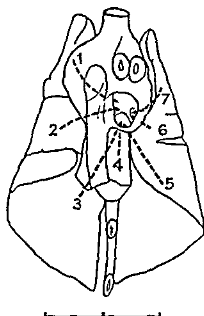


FIG 132 —*Outline drawing from fig 131* with approximate courses of main pulmonary veins indicated by interrupted lines Right group *formed by 1 and 2 the veins draining the right apical and cardiac lobes respectively these vessels* open into the left atrium in intimate relation to *the free or apposable portion of the via sinistra* Caudal group formed by *3 4* and 5 the veins draining the right diaphragmatic and intermediate *and the left diaphragmatic lobes respectively* Left group formed by *6* and *7* the veins draining the left cardiac and apical lobes respectively Scale *in* cm

into three lobes or equivalent masses In the equine and similar types, the masses have to be determined mainly by the vascular arrangements

The pulmonary venous drainage follows very closely the lobation , it is only very rarely, and even then only slightly, that any vein has encroached on what might be regarded as the territory of its neighbour

The pulmonary vein entries into the left atrium are arranged in three groups (right, caudal, and left), as in the lamb The right group is formed by the openings of the veins draining the right apical and cardiac lobes the caudal group by the openings of the veins draining the right and left diaphragmatic lobes and the lobus intermedius, and the left group by the openings of the veins

draining the left cardiac and apical lobes (see, e g, figs 131, 132) The right group and the via sinistra are intimately associated, as in the lamb, and a variable amount of the pars libera of the via is interposed between the left division of the posterior caval blood stream and the stream which flows in from the right apical and cardiac lobes (fig 133) The surround of the common opening is strong and the pars libera viae sinistrae tenuous so caeteris paribus, increased pulmonary inflow must be at the expense of the caval inflow, and vice versa This is very appropriate, for the caval inflow during intra-uterine life, performs a function that is fulfilled post natally, by the pulmonary veins i e it brings re oxygenated blood to the left atrium for distribution by the aorta That the other pulmonary streams aid in the functional closure of the via sinistra seems likely but it is normally only the right group of entries that has the special relation to the via In the African elephant foetus (fig 126) the relation still holds despite the fact that the whole of the pulmonary venous blood enters a special sinus and must flow past the pars libera viae sinistrae In the hippopotamus foetus the opening of the vein draining the right diaphragmatic lobe in addition to the openings of those draining the right cardiac and apical lobes is in the special relation to the via It is possible that the whale foetus is similar but a final report is not yet available

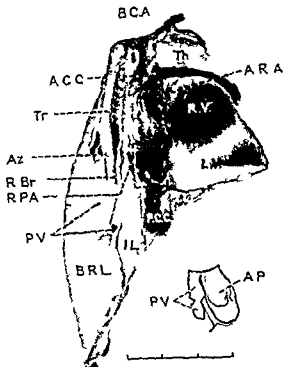


FIG 133—Horse foetus 141 over 335-345 days Right lateral view of thoracic viscera divided longitudinally and somewhat obliquely in the long axis of the posterior caval channel *P C C* To show that the dorsal part of the free portion *A P* of the via sinistra alone separates that channel from the pulmonary veins *P V* in inset draining the more cranial part of the right lung *B R L* body of right lung *I L* intermediate lobe of right lung *A C C* anterior caval channel *A R A* auricle of right atrium *R V L V* right and left ventricles *B C A* brachiocephalic artery *Tr* trachea *R Br* right bronchus *A* azygos vein *R P A* right pulmonary artery *P V* pulmonary veins *Th* thymus The inset is an enlarged outline of the part contained within the interrupted lines The via sinistra is closed Scale in cm

(ix) THE ANTERIOR CAVAL CHANNEL AND ITS RELATION TO THE VIA DEXTRA THE CRISTA INTERVENIENS

Bilateral anterior venae cavae persist regularly in some species of mammals and exceptionally in others (see Amoroso, Barclay, Franklin and Prichard, 1943) so some foetuses have two anterior caval channels, this is so, for instance in the specimens of *Loxodonta africana* and *Pteropus giganteus* personally

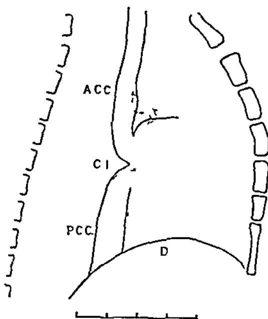


FIG 134—Goat foetus 136/147 days Outline drawing from two successive frames of direct cineradiographic record to show functional variation in shape of *CI* the crista interveniens (tubercle of Lower) The continuous line indicates the appearance in the first frame the interrupted line that in the second frame one third of a second later *ACC PCC* anterior and posterior caval channels *D* diaphragm Scale = cm on radiographic record

examined When there are two channels, the crista interveniens is the meeting point of the right one and the via dextra, and the left one has a *terminal course corresponding* with that of the main azygos vein and the coronary sinus in the lamb

It would be foreign to the purpose of this Chapter to give detailed accounts of *the right anterior caval channel in all the* mammalian foetuses studied, but as a rule it begins by passing nearly due caudally, then inclines to a greater or less extent to the right, and finally bends more or *less sternally, though still with some in*clination to the right, in the last part of its course In the living animal, it exhibits considerable variations in calibre during the different phases of the cardiac cycle

The via dextra, like the last part of the anterior caval channel, bends sternally to a different degree in different species, and the movements of the heart chambers cause physiological accentuations or reductions in the degree of the two bendings Hence there are functional (fig 134) as well as specific (cf figs 134, 135, 136) differences in the angle subtended by the crista interveniens, which may also vary in (amongst others) the following respects

(1) The inclination of its edge, viewed from the sternal and lateral aspects

(2) The character of its edge (sharp or obtuse, straight, or concave towards the sternum)

(3) Its provision of muscle fibres

(4) Its relation to the crista dividens

Personal findings are not yet extensive enough for one to make any useful generalizations about the crista interveniens, *but it is obvious that the* structure is of importance to the foetal circulatory story and the part which it plays in any particular species should be assessed as the course of the blood flow is determined in that species So far as the anatomical appearances go, the crista is most marked in the horse (fig 136) among the foetuses personally examined According to Tandler (1913), it is even more pronounced *in the seal* than in the horse, at least in so far as the adult is concerned

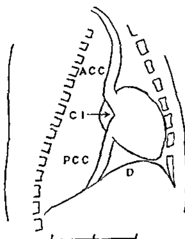


FIG 135—Kitten under 48 hours post partum Outline drawing from direct cineradiographic record to show angle of crista interveniens Lettering and scale as in fig 134

(x) THE AZYGOS VENOUS SYSTEM AND THE CORONARY SINUS

At a time when ideas about the azygos venous system are undergoing revision but the new ideas have not been fully published, it would be rash to attempt any detailed account of personal findings, and all that one need do is to stress the importance of including the azygos venous drainage in the foetal circulatory story of any particular species that one may be studying The omission of any reference to the system in most earlier schemata of the foetal circulation is surprising for the total azygos venous return must be an appreciable one In the lamb and in the kid, as in many similar animals, the greater part of the azygos drainage enters the heart via the coronary sinus and the smaller part flows in with the anterior caval stream In such animals and also in those with bilateral anterior venae cavae, the Thebesian valve is wanting

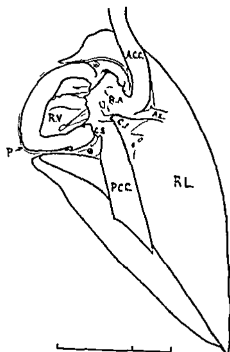


FIG 136—Horse foetus 141 days View of right half of thoracic viscera divided by a sterno-dorsal cut in the long axis of the posterior caval channel *PCC* To show angle of crista interveniens *CI* *ACC* anterior caval channel *A* azygos vein *RA* right atrium *RV* right ventricle *CS* coronary sinus opening *P* pericardium Projection of most cranial part of crista dividens which was in the other half of the specimen *RL* body of right lung Scale in cm

(xi) THE APEX OF THE HEART

In the vast majority of the foetuses personally examined the apex of the heart has been in or very close to, the sterno dorsal mid line of the body The most marked exceptions have been provided by the gorilla, the Indian fruit-bat (*Pteropus giganteus*) and the mole (*Talpa europaea*), the literature on the subject includes Daubenton (in Buffon and Daubenton 1766), Meckel (1831 296–7) and Tanja (1891) Regularly in some species, e g the dugong (Home 1823) the apex may be bifid, it is so in the African elephant foetus (fig 137) and to a less extent in the specimen of *Colobus occidentalis* (fig 138), in the present series In the majority of animals personally examined, the apex has been formed by the left ventricle only This (apart from other reasons) makes it difficult to assess the truth or otherwise of the statement that originated with Spigel (1626) namely, that in the foetus the two ventricles have walls of the same thickness For along what lines should one cut if one is to make the comparison in pari materia? It is easier to note disparity some time after birth than to be sure about intra uterine parity

(xii) THE PULMONARY TRUNK AND THE DUCTUS ARTERIOSUS

(1) *The pulmonary trunk*—Jean Mery, at the end of the seventeenth century and the beginning of the eighteenth, rightly stressed the fact that in the dead

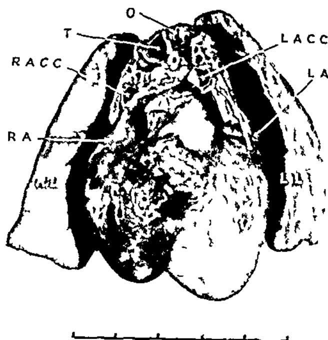


FIG 137 —*African elephant foetus (see fig 93)* Sternal view of thoracic viscera to show bifid apex of heart *R A L A* right and left atria *R V L V* right and left ventricles *P T* pulmonary trunk *A* aorta *R A C C L A C C* right and left anterior caval channels *R L L L* right and left lungs *T* trachea *O* oesophagus Scale in cm



FIG 138 —*Colobus occidentalis* foetus age unknown Sternal view of thoracic viscera to show bifid apex of heart *R V L V* right and left ventricles *A* aorta *I C C* inferior caval channel *O* oesophagus *Tr* trachea *Th* thymus Scale in cm

foetus the pulmonary trunk exceeds in calibre the first part of the aorta Radiographically, this preponderance has been fully demonstrated not only in the living foetal lamb, but also in the living foetal kid The significance, however, of the finding is not yet fully apparent

(2) *The ductus arteriosus* —The present writers have always felt that this structure was a special interest, on the functional side, of Barcroft and his Cambridge colleagues and, on the anatomical side, of Boyd It appears, however, that Boyd is concerned mainly with certain types of receptor end-organs and that his interest in the ductus is primarily due to the presence within it of such end-organs (personal communication, 1943) In consequence of the earlier misunderstanding, personal notes about the ductus in various foetuses have been less complete than they would otherwise have been, but a re-examination of a number of specimens has been of use in estimating the value of various statements found in the literature

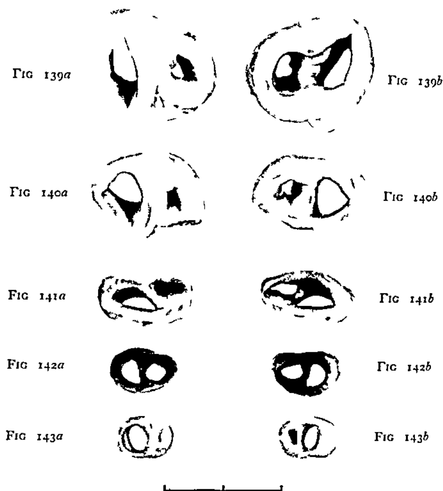
The things one needs to know about the channel are *its relative calibre, its* structure and nerve-supply, and details of its union with the aorta The relative calibre in the animals examined is much as already described for the lamb (Chapter III), i e the ductus is somewhat narrower than the pulmonary trunk before this latter has given off the pulmonary arteries, and more or less the same width as *the aorta after the latter has given off the vessels to the head* and anterior extremities, Kennedy and Clark (1941) gave details about the guinea-pig With slight differences in detail, the structure of the lamb's ductus reappears in that of the dog, cat, and rabbit (Boyd, 1941, 465), and also

in that of the guinea pig (Kennedy and Clark 1941), in brief, the *ductus* is a very muscular vessel and is in sharp contrast to the elastic vessels which it joins. With regard to the innervation, Boyd (1941) gave the following summary "The mammalian ductus *arteriosus* possesses a sensory innervation very similar to that possessed by the aorta and the carotid sinus. This nerve supply is derived from the left vagus nerve and, when it is present, from the left aortic nerve. Fine nerve fibres, presumably motor, are also found terminating in relation to the muscular coat of the ductus but the available material does not permit of a statement as to their origin. The distal portion of the pulmonary trunk and the proximal portions of the pulmonary arteries also possess a sparse afferent innervation." Kennedy and Clark (1941) admitted the presence of afferent and efferent nerve-fibres and nerve-endings in the wall of the guinea-pig's ductus, but considered that their presence was incidental to the location of the channel (i e that they were a spread-over from the neighbouring aorta, etc), and that the evidence was insufficient for an interpretation of their function.

The union of the ductus and aorta is a lateral anastomosis at a fairly acute angle; it results in a ridge somewhat like the crista *dividens* in reverse and could appropriately be styled *crista reuniens*. Since the time when this ridge was noticed by Zuntz (see Strassmann, 1894) in the lamb it has served as the anatomical basis for one of the hypotheses of the functional post natal closure of the ductus arteriosus. Strassmann saw Zuntz's findings in the lamb, and himself reported similar ones in Man, the dog and the cat. He postulated, on the strength of rather crude experiments, that after birth the pressure in the aorta rises above that in the ductus and causes the apposition of the flap like structure over the opening of the ductus. Graper (1921, 316–17) produced a very scathing criticism of Strassmann's work and of his hypothesis, and noted further (ibid 319) that the "spur" in the calf is several millimetres thick and is scarcely sharp edged. In 1935 however, Woodbury Hamilton and Woods reported the existence of a "functional valve" in the foetal rabbit, and later (Hamilton Woodbury and Woods, 1937) they wrote that the ductus entry is valve like in both the dog and the rabbit. In the former, they said, there is a single flap and in the latter a double flap (see their figs 9 and 10), in both species the 'valve' prevents the passage of a saline perfusion from the aorta into the ductus but not from the ductus into the aorta. Harman and Herbertson (1938) found no 'flap valve like structure' in the guinea pig, and Kennedy and Clark (1941) considered that the small fold or projecting lip present in this animal (see their fig 8) cannot be an important factor in the post-natal closure of the ductus.

The present writers, as noted in an earlier Chapter made a retrograde injection into the femoral artery of a moribund, but still living, foetal lamb and found that the injection passed as readily into the ductus as it did into the arch of the aorta. Nor was there any sign of a narrowing at the entry into the ductus from the aorta. They also examined the ridge in a number of fixed foetuses and newborn animals (see figs 139–143). In a (full term) gorilla foetus the ductus was patent and the ridge had a fairly sharp edge. In a lion cub which died about 24 hours after birth the ductus was narrower a little distance proximal to the ridge than it was at the level of the ridge itself. The same was true in a

newborn St Bernard puppy In a horse foetus (age not known, but of fair size), there was a noticeable narrowing of the ductus proximal to a ridge with a somewhat rounded edge (fig 140) In a stillborn tapir foetus (? age) the ductus was patent (fig 141) A foetal calf, aged 8 months (fig 139), showed a more rounded edge of the ridge, and somewhat less proximal constriction



Figs 139–143 —Views of aorta and ductus arteriosus from proximal (left series) and distal (right series) sides of their union In left series of views the aorta is on the left in right series it is on the right Scale in cm

Fig 139 —Bovine foetus 8 months

Fig 140 —Horse foetus age unknown

Fig 141 —Malay tapir foetus stillborn (see fig 92)

Fig 142 —Sheep foetus *c* 120/147 days delivered by Caesarean section Ductus arteriosus patent

Fig 143 —Sheep foetus 139/147 days delivered by Caesarean section Ductus arteriosus functionally closed

of the ductus, than did the foetal horse Finally, in one foetal lamb (*c* 120 days) the ductus was patent (fig 142) and in the other (139 days) it was completely closed proximal to the ridge (fig 143) A picture of the ridge in a goat foetus (136 days) has already been given (fig 124*a*)

If one summarizes the above personal findings, one may say that, where a constriction of the ductus exists, it tends to be some distance proximal to the ridge, at the level of the ridge itself the ductus is wide and in general there is

no suggestion that the ridge could be apposed, or is apposed, to effect functional closure of the channel In the dog the conditions of union of the ductus and aorta were different from those found in the other animals in that the two vessels ran alongside one another for an appreciable distance instead of converging on one another at a more or less acute angle In this species therefore one could imagine a rise of pressure in the aorta occluding somewhat the neighbouring channel but it would appear that constriction of the ductus, proximal to the ridge is the more probable mechanism, i e that the dog is like the other animals examined It is regretted that no rabbit foetuses were available, in view of Hamilton Woodbury and Woods findings in respect of this species To conclude this account, one may add that the edge of the crista reuniens, if one may use that term, tends to be crescentic in a lateral view, with the concavity of the crescent directed distally

CHAPTER VIII

Comparative Physiology

In this Chapter is collected information about the course of the foetal blood flow, about birth and the rupture or division of the umbilical cord, and about the post-natal functional closures of certain blood channels, in species other than *Ovis aries* To include other aspects of the comparative physiology would be difficult for reasons of space, and redundant in view of what others have already written (e g Barcroft, 1936, 1938, a , Windle, 1940, b) or are known to be in process of preparing for publication

(1) THE COURSE OF THE FOETAL BLOOD FLOW

Certain earlier work (Pohlman, 1907, 1909 , Kellogg, 1928, 1930) upon the course of the flow will get little more than this passing reference, for the experiments in question are generally held to have been superseded by later researches and they have already been mentioned in Chapter I On the other hand, as Windle and Becker (1940) pointed out, some of Kellogg's findings can be regarded as supporting the contention which he claimed to disprove , those interested should read Kellogg's account in the light of the more recent discoveries detailed below and in Chapter IV above

What remains, if one omits Pohlman and Kellogg's contributions, is contained (1) in a paper by Windle and Becker (1940) and (2) in hitherto unpublished records obtained by Barclay, Barcroft, Franklin and Prichard

(1) Windle and Becker described experiments which they had carried out upon foetal kittens and guinea-pigs, delivered with their placental circulations still intact and with pulmonary respiration prevented The guinea-pigs varied in age from 40 days to full term, the kittens from 54 to 60 days, the gestation time being about the same (67 days) for both species

In one group of experiments the colour of the blood in the exposed carotid arteries and jugular veins was compared with that of the blood in the umbilical vessels In a few foetuses of this group the thorax was rapidly opened and the heart examined for colour differences between its two sides In a second group of experiments, in which fourteen foetuses of each species were used, the heart and lungs were displayed rapidly and without haemorrhage, and the passage into them of Indian ink, injected into an umbilical vena comes, was observed directly, the distribution of the ink was usually checked by post mortem examination and histological section In a third group of experiments, in which eight guinea-pig and three cat foetuses were used, the procedure was similar, except that the injections were made into an external jugular vein

The results were as follows When the blood in the umbilical arteries was dark and that in the vein bright red, the carotid arteries were nearly as red as the umbilical vein, in other words, there could not have been any considerable mixing of the umbilical venous blood before its distribution to the head

Colour differences between the two sides of the heart, noted earlier by Barcroft (1936) in the guinea pig, were paralleled in Windle and Becker's experiments, in so far as the atria were concerned (it was only in the youngest foetuses that the ventricular walls were sufficiently transparent for observation, and then only at the apices) The left atrium was as brightly coloured as the umbilical vein, while the right atrium was as dark as the jugular veins

Indian ink injected into the umbilical vein passed first to the left atrium and left ventricle and thereafter to the aorta heart muscle, and brain If sufficient was injected, the return flow from the periphery darkened the lungs about 13 to 17 5 seconds later Indian ink injected into the jugular vein passed through the right side of the heart and the lungs before there was any darkening of the left side of the heart and the degree of darkening on this side was always less than that on the right side

The above results were obtained in foetuses with a vigorous heart beat In three guinea pigs and one kitten, in which the heart beat had become feeble, ink injected into either vena cava entered both atria slowly and at almost the same instant

The authors concluded that during the last third of gestation in the cat and guinea pig foetus, all or nearly all of the blood entering the heart by the posterior caval channel goes to the left atrium and left ventricle for distribution to the heart muscle brain and anterior parts of the body On the other hand, all or nearly all of the blood entering the heart by the anterior caval channel passes through the right atrium and right ventricle for distribution to the lungs and the posterior parts of the body, including the placenta The findings in animals with poorly beating hearts suggest an explanation of Pohlman's results and of the majority of Kellogg's results, actually, in one litter of puppies as Windle and Becker pointed out Kellogg's (1928) findings were more like those in the healthy kittens and guinea-pigs

Following the publication of Windle and Becker's findings Whitehead (1942) produced ' a working model of the crossing caval blood streams in the fetal right atrium the subject of the model was a mature kitten foetus While it is of interest to see such outcome of more recent work upon the foetal circulation one must point out that the caval streams are incorrectly described as crossing in the right atrium if one accepts the concept of the posterior caval channel bifurcating within the heart into a via sinistra and a via dextra

(2) In 1943 Barclay Barcroft, Franklin and Prichard recorded the course of the blood flow in the intact goat (*Capra hircus*) foetus by means of direct cine-radiography combined with intravenous injections of radio opaque medium (35 per cent perabrodil) The experiments were carried out at the Nuffield Institute and their main object was to show what effect, if any, section of both vagi would have upon the functional closure of the ductus arteriosus [1]

In view of the small number of foetuses studied one is scarcely justified in giving any extensive account of the results, but a short note is not out of place Two goats were delivered by Caesarean section under a combination of spinal and local anaesthesia The first goat had two kids, aged 136 days and weighing

[1] For permission to publish here and in section (iii) below an account of this joint work we are indebted to Sir Joseph Barcroft —A E B K J F M M L P

respectively 2087 and 2003 g , the second goat had one kid, aged 139 days and weighing 2850 g The gestation time is the same as that for the sheep, i e about 147 days

The vessels used for injection were the jugular and femoral veins and an umbilical vena comes, the jugular and femoral vessels were exposed under local anaesthesia for the insertion of cannulae The course of the blood flow was very similar to that in the foetal lamb, i e all the anterior caval blood went to the right side of the heart and was distributed to the pulmonary arteries and, via the ductus arteriosus, to the descending aorta, while the posterior caval flow went mainly to the left side of the heart If anything, the ductus venosus appeared to take more of the umbilical venous flow than it usually does in the lamb and more of the posterior caval flow went to the left heart But one cannot dogmatize about such differences on the basis of so small a series of observations, and the more important feature, in any case, is the fundamental similarity in the course of the blood flow in the two genera

The results so far obtained, in Oxford and Chicago respectively, can be regarded as a satisfactory beginning, but it is to be hoped that further studies will soon be made in respect of other genera and other orders of mammals For wide generalizations about the foetal blood flow cannot be made until the range of animals investigated has been very considerably extended

(ii) BIRTH AND THE RUPTURE OR DIVISION OF THE UMBILICAL CORD

In this section less attention is directed towards the general features of birth than towards the severance of the umbilical cord, for this latter is of major importance in the change-over from the foetal to the post-natal circulation The severance occurs in one of two ways, namely, by rupture or by division The former is what happens in species such as the horse and the ox, in which the cord is unable to support the weight of the foetus , it also occurs in some other species when the efforts of the newborn animal itself cause the severance Division of the cord, on the other hand, is effected in many species by the efforts of the mother In either rupture or division, the smooth musculature of the umbilical vessels is mechanically stimulated to a sufficient degree to effect their closure, and very little blood, or else none at all, escapes from their severed ends This is a very remarkable thing, and it should excite the interest of all those who are capable of appreciating an efficiently working mechanism

About the behaviour of wild animals in respect of the umbilical cord there is, apparently, no literature But a few notes about the behaviour of such animals in captivity have been furnished through the kindness of Dr G M Vevers, of the Zoological Society of London, and these notes are included in the account which follows

Placentophagia is of general occurrence (Lenkeit, 1929) In addition, animals which produce several young at a birth often eat stillborn foetuses and, on occasion, they may even kill their living newborn young and eat them (Williams, 1940) There is no obvious advantage of placentophagia unless, in wild life, it helps to prevent animals and birds of prey from scenting the new-

born In domestic animals the only disadvantage, namely, danger of choking, appears to be confined to the cow

After this general introduction one may pass to details about the individual species

Horse —The period of gestation given by various authors (St Cyr and von Oettingen quoted by Williams, 1940, Williams 1940, Wright, 1943) varies from 307 to 394 days

A very graphic description of foaling was given by Wright (1943) The account which follows here is based upon that description, but notice has also been taken of various other statements (Hofmann 1877, Bayer, 1900, Bucura 1902 Hauptmann 1911, Meyer 1914 a, Fleming, 1930, Williams, 1940) and of information received from Prof Formston

It should be remembered that the foal has a diffuse placenta, not too firmly attached to the uterus, and a relatively long and not over-strong umbilical cord The character of the placenta means that a partial separation of it during delivery of the foetus is prone to develop rapidly into a complete separation, with consequent asphyxia of the foal if it is still unable to breathe for itself The length of the cord usually makes it possible for the foal to be born with the cord intact the relative fragility results in rupture when the cord takes the weight of the foetus

The onset of the first stage of labour is usually indicated by "patchy" sweating, strong uterine contractions (more powerful and more continuous than in the cow according to Fleming) force the foetal sacs into and through the relaxed cervix and dilate it This stage may last from 1 to 4 hours and it terminates with the rupture of the allanto chorionic membrane and the escape of the allantoic fluid (under 2 litres) from the vulva The membrane thereafter remains as a moist lining within the vagina until the end of labour

The second stage begins suddenly with the appearance of the amniotic sac at the vulva or with the onset of straining, or with both together The mare usually goes down on to her side with her limbs extended The appearance of the water bag at the vulva is *rapidly* followed in most cases, by the appearance within it of a digit the second digit follows 12 5 to 15 cm behind the first This arrangement means that only one elbow at a time passes the pelvic outlet the lie of the two digits persists until the head neck, and fore-limbs have been delivered The amniotic sac is usually ruptured during the second stage of labour by the pressure of digits or by the weight of the foetal head and chest, or by the trunk when it ' flops ' out of the vagina The foal commences to breathe so soon as its nostrils are in contact with air, irrespective of whether or not it is yet completely born With the onset of respiration according to Williams the pulsation of the umbilical arteries diminishes and soon ceases altogether but it is not impossible that the cord is itself somewhat compressed at this stage in some labours and that such compression helps to initiate respiration The mare ceases to strain once the foetal hips have been delivered and the hind limbs are not withdrawn from the vagina until the foal moves or the mare rises The umbilical cord is usually intact when the foal has just been born The duration of the second stage of labour may be from 9 to 70 minutes, but is usually 30 minutes or less (Wright), Fleming gives the

time as 5 to 15 minutes, and Williams as 15 to 30 minutes The rupture of the umbilical cord usually occurs as the result of post partum movement of the foetus, or of the mare rising or turning towards the foal or moving away from it More rarely, in a standing birth, a relatively short cord may be ruptured by the weight of the foal as it falls (Bayer, 1900) The traction on the cord, according to Hauptmann (1911), mechanically stimulates both the musculature of the umbilical arteries and also the ring of smooth muscle surrounding the vessels in the neck of cord just distal to the umbilicus (i e just distal to what Williams called the "umbilical base" or "cutaneous navel"—a hairless, cylindrical, firm segment 2 5 to 3 75 cm long) The contraction of the arterial and the ring musculature causes a local diminution in calibre of the cord In addition, the contracted ring musculature grips the umbilical vessels very firmly in preparation for their impending rupture The effects of this are seen externally as an indentation just next to the junction of the cord with the skin—the muscle ring is most developed at this point—and also as fine longitudinal furrows in the cord epithelium overlying the muscle The site of rupture is at or near to the distal edge of the ring (Fleming said it is usually 5 cm, sometimes as much as 15 cm, from the umbilicus, Williams gave the distance as 3 75 to 5 cm from the same point, Wright said 5 to 7 5 cm below the foal's belly) Fugger (1578, quoted by Hauptmann) said that the amount of blood lost was a few drops to half a spoonful, and generally it is not much, Franck (quoted by Bayer) put the upper limit at 250 c c, but such an amount is presumably not common Roll told Hofmann that he had never seen haemorrhage from the remains of the foal's cord In general, the figure is lower the greater the tug on the cord before rupture If the tug is absent altogether, i e if the cord has to be divided by scissors in assisted birth, excessive haemorrhage can be prevented only by tying the cord (Bucura)

The expulsion of the foal is an extreme effort for the mare and she usually rests for 12 to 30 minutes afterwards, occasionally she recovers more rapidly or more slowly than this

The third stage of labour is usually short, but may be prolonged Williams gave the duration as 15 to 30 minutes In one of Wright's cases the placenta separated during the birth of the foetus and part of the allantois-chorion was expelled round the foal In another case, however, the time was between 14 and 21 hours Normally, according to Wright, the membranes are inverted by the descending uterine contractions

The mare may eat the afterbirth, if it is not removed from her reach, but she shows less tendency than other animals to do this (Stoss, 1928, quoted by Williams)

Variations from the above picture of foaling can be found in the literature, but they are of little consequence to the present story

Like the young of other mammals which as a rule bear but one foetus per pregnancy, the foal is born very mature and within an hour from birth is on its feet and walking or running about (Williams)

Cow—Williams (1940), whose physiological standards were derived from findings in beef cattle rather than in dairy cattle, gave the duration of gestation as 285 ± 5 days

The account of calving which follows is based upon the literature (Bayer, 1900 de Bruin, 1901 Henneberg, 1902 Hauptmann, 1911, Meyer, 1914, a, Fleming 1930, Williams 1940), upon the experience of J Yule Bogue (over 200 cases of difficult birth), and upon information given by Prof Formston

It should be remembered that the calf has a cotyledonary placenta, fairly firmly attached to the uterus and a relatively short and not over-strong umbilical cord The character of the placenta means that a partial separation of it during delivery of the foetus is unlikely to develop rapidly into a complete separation, with consequent asphyxia of the calf The shortness and comparative fragility of the cord mean that it is usually ruptured by tension before the calf is completely born i e that respiration begins early and that the last part of the second stage of labour must be rapid if the calf is not to undergo dyspnoea and possibly asphyxia Further, it is obvious that the amniotic sac must be artificially ruptured by a certain time if it has not already burst naturally Otherwise, the first inspirations of the calf will draw amniotic fluid instead of air into its respiratory tract

Different authorities have different views about the position more commonly adopted by the cow during labour, Formston's opinion is that the standing and recumbent positions are about equally popular The length of the first stage is not given with any degree of precision, during it the cow is agitated and bellows, but the pains are not so powerful or continuous as in the mare (Fleming)

In the second stage the first foetal parts to present are usually the fore feet followed by the muzzle lying above the metacarpus (Fleming) By the time the head is in the vagina one can feel the foetus attempting to gasp, though the inspiratory phase ends abruptly as if something prevented completion of the act The onset of pulmonary respiration is not at this stage due to cooling of a cutaneous surface, for the surfaces are still warm and in addition, douching of the head with cold water will not evoke respiration The cause of the breathing is compression or rupture of the cord, i e arrest or cessation of the placental circulation Once the shoulders are born however douching of the head with cold water will evoke a reflex respiration The above account, which is given by Bogue does not quite correspond with that given by de Bruin in so far as the type of respiration is concerned [1] The difference may be due to the fact that Bogue's cases were dystocic De Bruin said that the first respiratory movement is a slow inspiration, accompanied by rales on account of the presence of amniotic fluid in the respiratory tract A few moments later, slimy masses are expectorated and the respiratory movements increase in rate but decrease in depth It is conceivable that Bogue found Lumsden's lowest type of respiration i e gasping, while de Bruin, in more normal births, described the apneustic type passing over into the pneumotaxic type If so there is a parallel in Barcroft's experience during a variety of human births (see Chapter XI) The rupture of the cord occurs within a very short distance from the umbilicus and is followed as the anatomical features in

[1] Obviously too the position the foetus has reached by the time the cord ruptures is subject to individual variations

ruminants would suggest (see Chapter VII), by the rapid contraction of the umbilical arteries and by their retraction through the umbilical ring into the abdomen There is either negligible haemorrhage or else none at all The umbilical vein tears at the umbilicus, and its torn end is conical and full of blood, the intra-abdominal portion often contains a clot (Kehrer, quoted by de Bruin, 77) Alternatively, the tear may occur slightly more peripherally and affect the venae comites, in this case the structure hanging from the umbilicus after birth consists of part of the sheath of the cord and the remains of the venae comites (de Bruin, 23) The duration of parturition is usually 1 to 2 hours, but it may be only 15 minutes or it may be extended, without injury to the calf, for 1 to 2 days, according to Fleming One of Williams' rules (rarely obeyed by dairy cows) for physiological birth was that the foetus should be expelled, without human aid, within one hour from the commencement of labour Formston says that the second stage lasts from 30 minutes to 3 hours if the cow has calved before, but that a heifer takes 6 to 7 hours

The cow licks the umbilical stump and skin of the newborn calf, turning it over with her horns to complete the process (de Bruin, Meyer) the licking helps to stimulate respiration (de Bruin)

The third stage, according to another of Williams' rules, should not last more than an hour In beef cattle his impression was that it usually took 30 minutes or less for completion In dairy cows it is occasionally over within 30 minutes, but usually lasts 1 to 3 hours, and may last 15 or 16 days, Fleming's figures are more or less the same On occasion, owing to the firm placental attachments, there may be retention, the percentage in Bogue's cases was about five

Placentophagia is frequent, but not invariable, if no measures are taken to prevent it It may lead to choking

The calf is born very mature, and is normally on its legs, and walking or running about, within an hour from birth

Pig —The pig has a diffuse placenta and a relatively very long cord In the semi-wild state the sow builds a mound of coarse grass, weeds or brush as a birth-bed, but in the domesticated state she accepts any substitute available (Williams, 1940) The description of farrowing varies considerably in different accounts, but all writers agree that the cord undergoes considerable mechanical stimulation (traction or biting) during its division

The sow farrows lying on her side (Fleming) The first stage of labour, according to Stoss (1928, quoted by Williams, 1940), takes from 2 to 6 hours, and the second stage (total for all the births) a similar time Fleming, however, said that not infrequently ten porkers are born in an hour, and the present writers know of a case in which thirteen were born in 40 minutes

According to Bayer (1900), the porker, and not the sow, divides the cord after birth He plants himself firmly on all fours and pulls at it, if this procedure is not successful, he puts one hind-leg on it and stretches and tugs until it ruptures Henneberg (1902) said that either the sow bites through the cord as she eats the membranes, etc, or else the porker stands on the membranes and pulls until the cord ruptures

Carnivores —The placentae of the puppy and kitten are local and zonary (Fleming), the cords are, relatively, of medium length and very strong The

following account of pupping or whelping and of kittening, is derived from a number of statements in the literature (Hofmann 1877, Bayer, 1900, Henneberg 1902, Bucura, 1902, Hauptmann 1911, Meyer, 1914, a, Fleming, 1930)

Both the bitch and the cat prepare a special nest to receive their young No details appear to be available about the first stage of labour The mother gives birth lying on her side with her head directed caudally, i e each foetus as it issues from the vulva is within reach of the mother's mouth The head of the foetus usually presents, the fore limbs often lie beside or under the foetal chest As the shoulders are born, the mother often utters a cry When birth is complete the mother bites through the membranes if they are still intact and then consumes them and the placenta and the cord nearly up to the umbilicus In the case of the puppy, in particular, the process is a severe one (Meyer) The bitch repeatedly rolls the newborn animal on to its side in her efforts to lick bite and gnaw at the stump of the cord The tension on the abdominal wall is severe repeated and prolonged far beyond the duration of a jerk In fact, the process usually appears so fraught with peril to the puppy that the observer feels inclined to interfere Obviously the mechanical stimulation to the vessels of the cord is very great and well calculated to cause them to constrict and prevent haemorrhage Hofmann, however, claimed that there was no greater loss of blood when the cord was divided by a knife or pair of scissors than when it was subjected to the more natural division Henneberg thought that perhaps Hofmann was unaware of the effect of traction on the cord and so (?) did not take care to avoid it in his experiments, it is also conceivable that cutting a cord of such relative toughness causes sufficient mechanical stimulation of the vessels

Rat, rabbit, guinea pig —According to Henneberg (1902), the rat foetus is born with its membranes intact The mother holds the newborn animal between her fore feet and consumes the membranes and placenta, and the tensed umbilical cord up to the umbilicus According to Meyer (1914, a), the rabbit and guinea pig also eat the placenta and bite or gnaw off the cord

Zoo animals —Almost all the primate births occur at night when usually no one is about Dr Vevers was present at three chimpanzee births and in each case the cord broke about one third of its length away from the infant There was no appreciable amount of haemorrhage In a fourth birth the cord and placenta were attached to the infant for three days before the mother allowed the keeper to approach near enough to cut the cord Dr Vevers has never seen a chimpanzee eat any of the placenta but they do imbibe a certain amount of the juices present at the birth The keeper in charge of the baboons has noted a number of cases in which the cord was attached for several hours after birth The carnivores deal with the cord much as the domesticated varieties do

(iii) THE FUNCTIONAL CLOSURES OF THE UMBILICAL VESSELS, THE VIA SINISTRA AND THE DUCTUS ARTERIOSUS

The story which follows is confined to the post natal functional closures mentioned in the title, because the lamb is the only animal in which other

closures have so far been studied. Comparison should be made with what is known about the lamb (Chapter VI) and about the human subject (Chapter XII).

(1) *The functional closures of the umbilical vessels.*—It is fitting to begin with these, for they are directly connected with the events described in the previous section, and are also the most obvious and most important of all the closures. If the umbilical vessels do not shut down rapidly after rupture or division of the cord, the newborn animal will bleed to death; a patent via sinistra or ductus arteriosus, on the other hand, is not incompatible with life (e.g. Beattie and Morton, 1939, found both conditions present together in a mature sheep).

When one looks through the literature, one finds very little about the closure of the umbilical vein and it may, therefore, be simplest to summarize here what is known about it before passing on to the much more copious detail about the arterial closures. Structurally, the veins in the cord are much more muscular and contractile than the intra-abdominal veins or vein. In the horse and ruminants (Meyer, 1914, a) the character of the cord matrix allows, in addition to contraction, retraction towards the umbilical ring; in other animals, the cord is normally divided so close up to the umbilicus that the inability of the veins to retract probably does not matter. The greater contractility and strength of the more peripheral portions of the umbilical venous channel ensure that the contained blood will move in the direction of the heart. The occlusion of the extra-abdominal portions, in personal experience, is as effective as that of the corresponding portions of the arteries; indeed, it is not easy to distinguish contracted veins from contracted arteries in the cord, and one usually has to follow them into the abdomen in order to be certain. Once the severed ends of the umbilical venae comites have contracted down, they should be able, without difficulty, to withstand any rise in venous pressure that is likely to occur. In the horse, the torn end of the vein in the cord may gape a little, but the vessel is completely impervious where it is enclosed in the special ring of smooth muscle at the cord-skin junction (Hauptmann, 1911).

The closure of the umbilical arteries is caused by contraction of the smooth muscle in response to a stimulus or stimuli; in immature foetuses the response is inadequate (Hofmann, 1877). Exner (1877, quoted by Bucura and others) said that the longitudinal musculature of the umbilical artery is sufficiently wide, in relation to the radius of the vessel, to produce vasoconstriction when it contracts; the effect is aided by the presence, external to the longitudinal musculature, of a strong circular layer. In the foetal state the inner surface of the vessel is smooth and even but, on their contraction, the longitudinal bundles increase in thickness and encroach upon the lumen until it disappears. The stimulus which evokes the contraction of the arterial musculature has not been finally determined; it may be different in different animals, and it is possible that more than one stimulus may act at a time.

Schultze (1871) and many of his successors believed that one of the factors concerned was a fall of pressure in the abdominal aorta coincident with the onset of respiration and the occlusion of the ductus arteriosus. These occurrences were held to divert an appreciable extra amount of blood to the expanding lungs and, in addition, the right ventricle no longer contributed to the mainten-

ance of the aortic pressure In consequence, it was thought, it was easier for the umbilical arteries to close Hofmann (1877) got von Basch to measure the pressures in newborn puppies and adult dogs and thought that the results supported the view that the pressure fell at birth Actually, they did not prove any such thing and Cohnstein and Zuntz (1888) later produced evidence favouring if anything the view that the pressure rises slightly after birth in the lamb They also showed (1884) that an appreciable amount of blood can be transferred from the placenta and cord to the newborn animal if ligation is delayed So any increase in the volume of the pulmonary vascular bed should be more than counterbalanced

Williams (1940) wrote that, so soon as the newborn foal breathes, the pulsation in the umbilical arteries at once diminishes and soon ceases, intrinsic forces have made provision against possible loss of blood before the impending rupture of the cord has occurred But there is evidence, in other animals, that the arteries of the cord are not affected by the onset of respiration In puppies Hofmann (1877) found that these vessels could not be reopened, once they had contracted by interruption of respiration, though the intra abdominal portions of the same vessels relaxed during the interruption and contracted down again when it ceased Bucura's (1902) experiment no 6 is also instructive He removed a rabbit foetus from the uterus, opened the membranes without disturbing the placental circulation, and then left the animal in the abdomen of its mother to prevent any effects of fall of temperature Under these conditions, there was no contraction of the umbilical arteries up to three hours from the onset of respiration at that point the experiment was terminated Nowadays it is well recognized among those who do foetal research that the placental circulation adequately safeguarded from mechanical stimuli and from changes of temperature, can be preserved for a long time after breathing has commenced On the other hand, compression or ligation of the cord is rapidly followed in animal experiments by the onset of respiration

Contraction of the cord arteries follows mechanical and electrical stimuli and cooling It is necessary to summarize the evidence and then to consider what parts mechanical insults and cooling play in the closure under natural conditions

One may begin with mechanical stimuli Hofmann (1877) found in puppies delivered by Caesarean section, that there was no haemorrhage from the cut ends though pulsation continued proximal to the cut This shows that the response is localized Henneberg (1902) worked on rat foetuses and noted that the umbilical arteries bled profusely after being cut if traction on the cord was avoided and cooling of it prevented On the other hand if the mother gnawed through the cord or if Henneberg himself stretched it before cutting through it, then the mechanical stimulus produced so strong a contraction of the arterial musculature that it did not subsequently relax in a warm bath Bucura (1902) found that the cutting of a puppy's cord led to a certain amount of haemorrhage, whereas the tearing of it was followed by no loss of blood The effects of mechanical stimuli are particularly interesting in the case of the foal Fugger (1578, quoted by Hauptmann, 1911) noted that some veterinary practitioners did not hold with ligating the cord in cases of haemorrhage,

instead, they were accustomed to take a few turns of the cord round one hand, to plant the left foot or both feet upon the abdomen of the recumbent foal, and with a strong, sharp tug to rupture the cord flush with the umbilicus This apparently brutal procedure was effective in arresting haemorrhage, and actually simulated the tug that normally occurs during birth of the foal Hauptmann himself found that there was excessive pulsatile haemorrhage when the natural mechanical stimulus was excluded and the arteries were divided with a sharp knife, if, however, the remains of the cord were subsequently given a sharp jerk and rupture was thereby produced at the normal site, the haemorrhage ceased When, thereafter, he excised the insertion of the cord with a knife, the arteries proximal to it were found to be full of blood and pulsating So it seems beyond dispute that the functional occlusion in the foal occurs at the cord-skin junction as a result of a very considerable and sudden mechanical stimulus It has already been noted that the musculature which is stimulated is not only that of the arteries and vein themselves, but also the strong ring of smooth muscle that surrounds them at this point in the foal

Effects of temperature changes upon the cord vessels have been recorded by a number of observers Hofmann (1877) said that theoretically exposure of the cord to cold air or water should result in vasoconstriction On the other hand, he thought it questionable if warmth favours haemorrhage from the divided vessels, for he had found that there was none, in puppies, when the foetal ends of the cords were immersed in a warm bath Henneberg (1902) thought that Hofmann must, unconsciously, have stimulated the arteries mechanically to such an extent that they would not subsequently respond to a rise in the temperature of their surrounding medium Henneberg himself experimented with newborn rats and found that there was copious haemorrhage from the divided cords if, immediately after birth, the animals were placed in a warm bath with their heads above the surface On the other hand, if the arteries were allowed to contract down before the animals were put into the bath, they did not relax as a result of the warmth Bucura (1902), in experiments upon rabbit and dog foetuses, showed that the relatively slight haemorrhage from the divided cord was arrested when it was dipped into cold water and increased when it was dipped into warm water

The same worker also studied the effects of electrical stimulation Weak induced currents caused localized contraction of the divided rabbit's cord and consequent arrest of the slight haemorrhage that had been occurring from it They also arrested the much greater haemorrhage evoked by the immersion in warm water of the divided puppy's cord The effects are what one would expect and their main interest lies in the localized nature of the response

The relative importance of cooling and of mechanical stimuli must be assessed in relation to the natural processes of birth in the different animals The severed arteries of ruminants retract rapidly through the umbilical ring and cooling is completely excluded from the picture of arterial closure in these animals In the horse it is possible that cooling may aid in effecting contraction, but the main stimulus is undoubtedly the strong tug which leads to rupture of the cord In respect of various other animals it should not be

difficult for the reader to estimate how far the mechanical stimulation, described in the previous section of this Chapter, is aided in any particular case by exposure of the cord, after birth, to the atmospheric air

The reactions of the intra-abdominal portions of the umbilical arteries have not been at all extensively studied Hofmann (1877) found in puppies, that the more proximal stretches (i e up to where the superior vesical arteries are given off) remained full of blood and pulsated, but that the more distal stretches commenced to close down at their umbilical ends between 4 and 24 hours after birth, and were completely closed on the second day after birth If the abdomen was opened immediately or soon after birth, these distal stretches rapidly became empty of blood and ceased to pulsate in consequence, Hofmann thought, of their exposure to atmospheric air If respiration was interrupted by pressure on the trachea, the contraction passed off but it reappeared so soon as the hindrance to respiration was removed The effect of opening of the abdomen upon the proximal stretches of the umbilical arteries was to cause a progressive decline in the intensity of their pulsation up to the death of the animal, one need not presumably, regard this as a specific effect upon these particular vessels it was more likely local evidence of a general circulatory failure consequent upon the laparotomy and exposure The only other experimental observation is that of Hauptmann (1911) who found the intra abdominal portions of the foal s arteries pulsating and full of blood just proximal to the site of functional post natal occlusion of the cord vessels

(2) *Functional closures of the via sinistra and the ductus arteriosus* —Indirect evidence about the closures of the via sinistra and ductus arteriosus, together with some evidence about the possible mechanism of the latter, was provided by Woodbury, Hamilton and Woods (1935), and by Hamilton Woodbury and Woods (1937) Later more direct observations were made of the closure of the ductus arteriosus first by Barcroft, Kennedy and Mason (1938), then by Kennedy and Clark (1941, 1942, see also Kennedy, 1942), and finally by Barclay, Barcroft, Franklin and Prichard (1943, unpublished) Reference should also be made to the review by Barron (1944), which appeared too late for that author s views to be incorporated in this section

In their brief note of 1935 Woodbury, Hamilton and Woods summarized the results of experiments in which they had taken simultaneous records of right and left ventricular pressures in unoperated rabbit foetuses Before the onset of respiration and during the first expirations the pressures on the two sides of the heart were nearly equal, but with each early expansion of the lungs the right ventricular pressure was reduced by a half while the left remained relatively constant throughout the respiratory cycle The authors concluded that the fall in the right ventricular pressure was due to decreased pulmonary resistance and that the inequality between the two pressures during inspiration pointed to the existence of a functional valve in the ductus arteriosus, the presence of such a valve was shown at autopsy After the lungs had become expanded respiration caused small changes in the right ventricular pressure and expiration improved the filling of the left heart, as shown by marked rises in both diastolic and systolic pressure values The via sinistra was found to be functionally closed a few hours after birth

In their longer account of 1937, the same authors described their work upon dog and rabbit foetuses, delivered through the abdominal wall. The operation caused detachment of the placentae in the cases of the rabbits, but in the cases of the dogs the placentae were often retained throughout the experiment. If, in view of the doubts the authors themselves expressed on pp. 207 and 209, one omits the effects of clamping of the cord, the results may be summarized as follows. "Intraventricular pressures were taken from the right and left ventricles of immature and mature dog and rabbit foetuses immediately upon delivery, ... when the fetus first breathed, and during the first two days of independent life." Right and left ventricular pressures were similar before the onset of respiration, and lower in the immature foetuses than in the mature ones. Inspiration lowered the right ventricular pressure more than the left, and the pressure relationships were such that the authors postulated an early functional closure of the via sinistra and ductus arteriosus in the species investigated.

The evidence for the functional closure of the ductus was, of course, the greater inspiratory drop in the right ventricular pressure, which could not have occurred had the channel been pervious. In the authors' view, the direct effect of inspiration was equal on both ventricles but the indirect one (lowering of peripheral resistance in the pulmonary circuit) affected the right ventricle only. Hence blood would have passed from the aorta into the ductus had nothing prevented such reflux. However, there was present in the dog a valve like single flap, and in the rabbit a double flap, which allowed perfusion of saline from the ductus into the aorta, but not in the opposite direction. So it was considered that functional closure of the channel resulted from the effect of the blood movement upon this flap or flaps, though the authors freely admitted that such a structure was not present in all species.

The evidence for functional closure of the via sinistra was somewhat more complicated and may, therefore, be given verbatim. "In the two day old rabbit illustrated in figure 12 the left auricular pressure has come well above the right. We suggest that this is because the left heart is responding to its increased work, according to Starling's law, with increased dilatation. The increased dilatation is consequent upon increased filling pressure and this in turn serves to close the foramen. It will probably remain closed until adherent. Later hypertrophy of the left ventricle will eliminate the necessity for dilatation and increased left filling pressure so that the adult relationship of similar auricular pressures in right and left heart will be attained. Intraventricular pressures in the unoperated adult range rather widely around the following figures: rabbit, L 140/0—R 25/0; dog, L 180/0—R 35/0.

"It should be emphasized that in accordance with modern conceptions of cardiac physiology a ventricle will hypertrophy if it works harder. However, it will work harder only if it is filled fuller either by residual blood left from previous increased contraction against a heavy load or by increased venous inflow. An increased filling requires an increased filling pressure. Thus it is difficult to explain even the beginning of hypertrophy of the left heart as compared to the right without postulating different filling pressures to the two hearts, and consequently an early functional closure of the foramen ovale."

To conclude this note one should point out that a contraction of the musculature of the ductus arteriosus remains a possible explanation of the functional closure of that channel in the dog and the rabbit, despite the finding of the "valve-like" flap or flaps by Hamilton, Woodbury and Woods Further, one must recall a legitimate criticism made by Abel and Windle (1939, 462), who wrote that "The blood pressure values which they give below their illustrations are not all in agreement with their statements in the text and would seem to indicate an increase in intraventricular pressures after respiration has begun"

The animal used by Barcroft, Kennedy and Mason (1938) and by Kennedy and Clark (1941 1942) in their studies of the closure of the ductus arteriosus was the guinea pig which is born in a very mature condition, and has blood vessels that are thin walled enough for one to judge of their internal calibre from their external appearance

Barcroft Kennedy and Mason found that stimulation of the distal end of the left vagus produced blanching of the ductus, especially of its aortic end, and slowing of the heart At the end of stimulation or on vagal escape the pressure in the pulmonary trunk returned a little while before the ductus relaxed Central stimulation of the right vagus, with the left one intact, caused no closure, and the result of distal stimulation of the right vagus was uncertain, if there was any constriction of the ductus, it was towards the cardiac end of the channel In one foetus, in which there was little slowing of the heart on stimulation of either nerve, the right vagus did not close the ductus, whereas the left one did In three perfusion experiments pilocarpine caused some constriction and in two of these the effect was reversed by atropine The authors apparently, concluded that the vagus nerve is related to the ductus arteriosus in the guinea pig for they pointed out that their findings did not rule out the possibility of an additional local mechanism being concerned in the closure of the channel They emphasized that pending further experiments their statements applied to guinea pigs alone

Kennedy and Clark s work formed a very definite advance upon the earlier experiments Their first paper was largely anatomical, but it also contained the beginning of the physiological story Mature foetuses were delivered into saline baths at body temperature and it was found that the ductus remained patent for several hours when the placenta and cord were kept intact and respiration was prevented the state of the ductus was observed through an opening made in the chest wall Temporary closure of the channel—apparently by muscular contraction—could be effected in various ways (rhythmic inflation of the lungs through a tracheal cannula, mechanical or weak electrical stimulation of the ductus wall) but reopening followed on cessation of the stimulus Closure also occurred if the foetus was allowed to breathe before the chest wall was opened, and the state of the placental circulation (intact or interrupted) was without influence upon the result The fact that the ductus was found closed in a series of animals ranging in age from a few minutes to 31 days post partum suggested that the closure was normally connected with pulmonary respiration To test this idea, several foetuses were brought to the surface of the saline bath had their cords clamped and were allowed to breathe

for varying periods before the state of the ductus was examined. It was found that partial closure occurred in 1 to 3 minutes, and complete closure in 4 to 10 minutes, from the onset of effective respiration.

In their second paper Kennedy and Clark repeated their view that the closure was effected by contraction of the smooth muscle in the wall of the ductus, unaided by the movement of any flap-like valve such as Hamilton, Woodbury and Woods found in the dog and the rabbit. They then went on to describe further experiments which they had undertaken with a view to discovering the reflexes responsible for the occlusion of the channel. They made use of their earlier finding that the ductus closes temporarily if the lungs are artificially inflated, and endeavoured by various means to interrupt the reflex pathways concerned.

They found, however, that they could not prevent closure by any of the following procedures (each was practised upon more than one foetus):

(*a*) Dissecting away the tissue on the anterior surface of the ductus, this tissue including the left vagus and phrenic nerves.

(*b*) Sectioning both vagi.

(*c*) Removing both stellate ganglia.

(*d*) Removing both stellate ganglia and sectioning both vagi.

(*e*) Ligating both carotid arteries below their bifurcations.

(*f*) Removing both carotid arteries including their bifurcations.

(*g*) Removing both carotid arteries including their bifurcations, and sectioning both vagi.

(*h*) Ligating very tightly all vessels, nerves and other structures of the mediastinum (except the trachea) cephalic to the aortic arch.

(*i*) Dividing the spinal cord at the third cervical, sixth thoracic, or ninth thoracic segment and destroying part of the cord on either side of the cut.

(*j*) Destroying large portions of the spinal cord, i.e. from the second cervical to the second thoracic, third cervical to the caudal end, and first thoracic to eleventh thoracic segment.

(*k*) Destroying the cord between the first and tenth thoracic segments and sectioning both vagi.

(*l*) Destroying all the cord from the second cervical segment to the caudal end, ligating all the mediastinal structures (except the trachea) cephalic to the aortic arch, and sectioning both vagi.

(*m*) Destroying the whole of the medulla and spinal cord, removing both stellate ganglia, and dividing both vagi.

The above procedures interrupted all known nervous pathways between the central nervous system and the region of the ductus, and there was no evidence to support the idea of a local reflex mechanism; finally, suitable electrical stimulation of the left vagus, right vagus, left cervical sympathetic, left phrenic, left stellate ganglion, and left splanchnic nerve was without any noticeable effect upon the ductus. "It appears from the above experiments," wrote the authors, "that a nerve pathway or a neuromuscular reflex is not essential for closure of the ductus. It also appears that the ductus will not close following stimulation of certain nerves which are anatomically closely associated with it."

The stimuli (other than artificial inflation of the lungs with air) which caused closure were

(a) Normal breathing

(b) Mechanical or electrical stimulation of the ductus This was effective in 15 to 30 seconds, i e it was more rapid than (a) above

(c) Artificial inflation of the lungs with oxygen, or with oxygen and nitrogen, but not with nitrogen alone

(d) Injection of adrenaline

(e) Mechanical stimulation of the left or right carotid sinus

(f) Haemorrhage The ductus closed in 6 minutes

(g) A number of miscellaneous stimuli, the method of action of which is not yet clear

(h) Intravenous injection of oxygen

The authors concluded that it is difficult to arrive at a conception of the cause of closure which will fit all the observed facts, but that under physiological conditions breathing is the most important stimulus , the gas mixture breathed, however, must contain oxygen

To end this section, one may mention the unpublished experiments of Barclay Barcroft, Franklin and Prichard (1943) upon goat foetuses It will be recalled (see section 1 above) that the first two kids were siblings of 136 days Number one had both vagi divided in the neck, a cannula inserted into the right jugular vein and a nose bag applied while it was still in utero After it had been delivered direct cineradiographic records were taken of four jugular vein injections made at intervals of ten minutes Immediately after the first injection the cord was tied and divided, and the healthy condition of the foetus was shown by the onset of bleating, efforts to stand, and so forth In the first shot the ductus was wide open and the pulmonary circuit time was 4 7 seconds In the second shot the lungs were transradiant through aëration, the ductus was closed and the left ventricle and aorta were well seen after 3 seconds i e the pulmonary circuit time had been considerably reduced In the third and fourth shots the ductus was still closed, and in the latter shot the pulmonary circuit time was under 2 7 seconds The time from ligation of the cord to the second shot, i e the time within which the ductus closed, was just under 9 minutes

The second foetus was delivered an hour after the first , the intra-uterine procedure was similar, except that the vagi were *not divided* The first shot was of a jugular vein injection with nose bag on and cord undivided , the ductus was wide open The nose bag was removed and the cord divided 5 5 minutes after this and a second jugular vein injection followed after a further 5 5 minutes The lungs were transradiant in this shot and the ductus was largely closed though there was a slight leak through it In the third and fourth jugular injections, 10 and 22 minutes respectively after the second, the ductus was closed and the pulmonary circuit time was under 2 7 seconds

So far then as one can judge from these two experiments, section of both vagi is without effect upon the closure of the ductus arteriosus in the newborn goat

In the third kid (age 139 days) the nose-bag was removed, for a special reason, 15 minutes before the cord was tied and divided The ductus was narrow though still patent 4 5 minutes from ligation of the cord, but it was functionally closed within 11 minutes from the same point of time [1]

[1] Sir Joseph Barcroft (personal communication) sends the following note about earlier experiments in which the present writers were not concerned In those experiments two sheep foetuses had both vagi cut just before delivery and they subsequently exhibited typical deep vagal respiration for twenty minutes at the end of which time they were killed The ductus immediately dissected out were found to be open It has however been his and our joint experience that a ductus closed for only a short time (as shown by X rays) may be found to be open post mortem

PART FIVE

THE HUMAN SUBJECT

CHAPTER IX

The Cardiovascular System of the Human Foetus

HOWEVER interesting and instructive work on lower animals may be, one's primary object in an Institute for Medical Research is to ascertain what happens in Man. Unfortunately many of the investigations which have been carried out in the living lamb either cannot be repeated, or else have not yet been repeated, in the human subject. Where the direct approach has not yet been made, and even more so where it can never be made, one has to compare the structural features in the respective cardiovascular systems and to assess how far similarity in structure is likely to be paralleled by similarity in functioning. The decision must be left with the individual reader, but he must be provided with such knowledge as is available and with such suggestions as are likely to assist him to come to a conclusion.

In addition to the purely anatomical data contained in the present Chapter, the three following ones contain such information as is available about the course of the blood flow, certain aspects of birth, and immediate post-natal changes. Inevitably, the part about which most has been written on the functional side is the umbilical cord, for this is the most accessible to sight and for experiment. A similar preponderance occurs in the anatomical literature but only in part for a similar reason. The other cause for the greater length of the section dealing with the structure, etc., of the human cord is the divergence of the various accounts of it. This divergence is not, in general, an indication that some authors have been less accurate than others in making their observations; rather, it is evidence of the extreme variability in structure exhibited by the individual specimens. It contrasts markedly with the similarity exhibited in all foetuses examined, by the crista dividens which, despite its importance, is adequately described in a short section illustrated by one or two figures.

The different parts of the cardiovascular system of the mature, or fairly mature, human foetus will be considered in this Chapter, in the following order:

(i) The placenta and its vessels.
(ii) The umbilical cord and its vessels.
(iii) The intra-abdominal portion of the umbilical vein.
(iv) The liver and the ductus venosus.
(v) The inferior caval channel and its terminal bifurcation.
(vi) The via sinistra and its pars libera.
(vii) The via dextra and its pars libera.
(viii) The coronary sinus and the Thebesian valve.

(ix) The heart
(x) The lobation of the lungs, the pulmonary veins and the relations of their openings to the via sinistra
(xi) The superior caval channel and its relation to the via dextra, the crista interveniens
(xii) The pulmonary trunk, ductus arteriosus, and aorta
(xiii) The arterial supply of the head and arms, the intra-abdominal portions of the umbilical arteries

(i) THE PLACENTA AND ITS VESSELS

(1) *The placenta* —The so-called "chorion" of Man is in fact an allanto chorion, and what is usually referred to as the placenta (and will so be in the rest of this account) is, properly speaking, the chorio-allantoic placenta As the classifications, etc, of such placentae have already been described in Chapter VII, section (i), this note about the human structure need not be over-long, it is essentially derived from Mossman (1937) The gross shape of the placenta is almost invariably discoid (fig 144) for, though many variations, e g double discoid, are known, they are all comparatively rare Again, though accessory placentae of varying sizes and number can be present, they are typically absent The placental type is villous, the endometrial relation deciduate, and the class, on the basis of finer structure, haemochorial (fig 147), in other words, the placental membrane, or layer separating the maternal blood from the foetal blood, consists entirely of foetal tissues (trophoblast, connective tissue, and endothelium) with no contribution at all from the maternal side The placental location is normally dorsal or ventral, rarely lateral or fundic



Fig 144 —Human foetus c 4½ months with umbilical cord placenta and membranes Scale in cm

(2) *The placental vessels* —Details about the placental vascular supply and its types are to be found in the papers by Shordania (1929, a) and by Bacsich and Smout (1938), figs 145 and 146 are reproduced, by courtesy of the authors, from this latter paper

(3) *The innervation of the placental vessels* —Fossati (1905) claimed that

these vessels were innervated, but it seems doubtful if he himself continued firm in his belief, and Bucura (1908) categorically denied the truth of it Schmitt (1922) said that no nerves had been found by previous workers and that his own results were equally negative Mabuchi (1924) on the other hand, reported the presence of non medullated fibres with free nerve-endings in the media, he also claimed that they were in process of development as early as the third month of gestation Ph Stohr jr (1928) reiterated that there was no innervation, and he was followed by Guarna (1934) who said that Fossati's fibre system was pre collagenous, and not nervous or collagenous If there are no nerve fibres in the umbilical cord, as Spivack (1943) concluded then a fortiori there are none in the placenta



FIG 145 —Human From Bacsich and Smout (1938) Distribution of umbilical vein in the placenta

(4) *The reactivity of the placental vessels* —This was studied by Lochmann (quoted by Henneberg, 1902) and by Henneberg Both found dilatation in response to certain forms of mechanical, chemical, and electrical stimuli, but modern methods of studying isolated organs and tissues were introduced after 1902 and the experiments need to be repeated before the findings can be accepted Schmitt (1922) reviewed the literature and himself (1929) reported spontaneous rhythmic contractions of placental vessels, but such movements are typical of most isolated smooth muscle preparations Oxygen causes contraction and lack of it relaxation (Schmitt, 1922, 1923, 1925, von Frey, 1923, Budelmann, 1929, Ueda, 1931, b), but again such effects are not peculiar to the placental vessels (Budelmann, 1929), Schmitt attributed them to pH changes consequent upon aerobic and anaerobic activity respectively Von Euler (1938), on a somewhat inadequate basis reported an absence of differences in reaction referable to the state of oxygenation of the perfusing solution Like Schmitt



FIG 146 —Human From Bacsich and Smout (1938) Arteries and vein of placenta injected with different colours to show their respective relations

(ix) The heart

(x) The lobation of the lungs, the pulmonary veins and the relations of their openings to the via sinistra

(xi) The superior caval channel and its relation to the via dextra, the crista interveniens

(xii) The pulmonary trunk, ductus arteriosus, and aorta

(xiii) The arterial supply of the head and arms, the intra-abdominal portions of the umbilical arteries

(i) THE PLACENTA AND ITS VESSELS

(1) *The placenta* —The so-called "chorion" of Man is in fact an allanto chorion, and what is usually referred to as the placenta (and will so be in the rest of this account) is, properly speaking, the chorio-allantoic placenta As the classifications, etc, of such placentae have already been described in Chapter VII, section (i), this note about the human structure need not be over-long, it is essentially derived from Mossman (1937) The gross shape of the placenta is almost invariably discoid (fig 144) for, though many variations, e g double discoid, are known, they are all comparatively rare Again, though accessory placentae of varying sizes and number can be present, they are typically absent The placental type is villous, the endometrial relation deciduate, and the class, on the basis of finer structure, haemochorial (fig 147), in other words, the placental membrane, or layer separating the maternal blood from the foetal blood, consists entirely of foetal tissues (trophoblast, connective tissue, and endothelium) with no contribution at all from the maternal side The placental location is normally dorsal or ventral, rarely lateral or fundic



FIG 144 —Human foetus c 4½ months with umbilical cord placenta and membranes Scale in cm

(2) *The placental vessels* —Details about the placental vascular supply and its types are to be found in the papers by Shordania (1929, a) and by Bacsich and Smout (1938), figs 145 and 146 are reproduced, by courtesy of the authors, from this latter paper

(3) *The innervation of the placental vessels* —Fossati (1905) claimed that

mann's earlier (1929) finding with ergotamine Ueda (1931, a) found dilatation with concentrations of pilocarpine over 1 in 100,000, and of acetylcholine between 1 in 20,000 and 1 in 5,000, with concentrations above this last there was a very acute dilatation followed by a slow constriction Atropine (Ueda, 1931, b) was without effect per se, but neutralized the actions of pilocarpine With acetylcholine von Euler (1938) usually obtained no effect or a weak dilatation, or else a pronounced constriction potentiated by eserine and abolished by atropine On the basis of all the evidence, it seems reasonable to suppose that the placental vessels are not innervated but that in the latter part of gestation their muscle cells acquire to a varying degree, something akin to Langley's "receptive substances," thus allowing relatively feeble responses to the autonomic drugs

(ii) THE UMBILICAL CORD AND ITS VESSELS

There is a vast literature upon the human umbilical cord partly because of its accessibility for study, partly because of the importance of the vessels enclosed in it and partly because of the great variations of structure and so forth exhibited by these vessels Fortunately, Shordania (1929 b) gave a fairly comprehensive general account and Spivack (1936, 1943) produced two very useful statements about special features (the "valves of Hoboken" and the innervation) The following survey is based upon these and nearly forty other articles, further references can be found by those interested, in the bibliographies appended to these articles

1 *External features of the cord*—The most striking one is its spirality Shordania found that right and left windings were equally frequent, and that the number of spirals (1 to 22) was not directly related to cord length The skin sometimes ends flush with the abdominal wall, sometimes projects up to 2 cm beyond it (Robin, 1860) The stub to which the proximal (foetal) end of the cord is attached tends to project farther from the abdomen on its cranial than on its caudal aspect (Tait, 1876)

2 *Length and width of the cord*—Shordania said that the lengths recorded in the literature varied from 0 to 300 cm In his own series of 421 cords, the range was from 35 to 104 cm, and the average 60 cm There was no regular relation between cord length and the weight of the foetus plus placenta As the foetal length is about 50 cm it is obvious that the average human cord is relatively longer than that of any animal mentioned in Chapter VII

The widths of 167 cords were measured by Shordania In the proximal, middle and distal thirds the ranges were respectively 1 0 to 1 8 cm, 0 7 to 1 6 cm and 0 8 to 1 5 cm with typical means of 1 2, 1 0, and 1 1 cm But in about 11 per cent there was a progressive fall in width from the umbilicus (1 6 cm) to the placenta (0 8 cm) Apart from the general variations in calibre noted above, individual cords often showed localized narrowings

3 *Strength of cord*—According to Bayer (1900) a forensic case led to the first investigations of the breaking strain of the human cord (Negrier, 1841), Chiari Braun and Spath (1855) made further measurements and Goenner and Kehrer (see Shordania) reported values of about 6 kg Shordania tested

(1922) and others, he found the placental vessels especially sensitive to thermal changes, constricting at low temperatures and dilating at high ones

(5) *The pharmacology of the placental vessels* —The reactions to drugs have been investigated in perfusion experiments (certain points of technique were stressed by Kustner and Siedentopf, 1929, a, b, and by Budelmann, 1929) and in experiments with isolated preparations There are the expected reactions to pH changes (Schmitt, 1923, Ordynsky, 1931), and to direct stimulants and depressants of smooth muscle (Schmitt, 1922, 1923, Kustner and Siedentopf, 1930, Ordynsky, 1931, Ueda, 1931, a, b, and, to some extent, von Euler, 1938), the main interest is, therefore, the light that may be thrown, through the reactions to autonomic drugs, upon the account of the innervation given by the histologists All the relevant literature has not been accessible to the present writers, but even so the results are not too readily co-ordinated into a simple story

So far as adrenaline is concerned, the relevant information is given in a

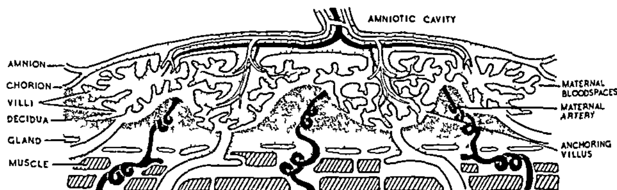


FIG 147 —Human Diagram (modified by Amoroso from Hertwig and Cowdry) of the mature placenta To show the relationship of the chorionic villi to the maternal circulation (see text)

number of papers (Schmitt, 1922, Budelmann, 1929, Kustner and Siedentopf, 1930, Ueda, 1931, a, Ordynsky, 1931, von Euler, 1938), and in general it indicates that the placental vessels, in the latter part of gestation exhibit a somewhat weak constrictor response For instance, the threshold concentrations reported by Ueda and Ordynsky respectively were 1 in 10, and 1 in 5, millions, and Ordynsky said that the vessels of the human finger, which he studied as a control, were far more sensitive [1] Von Euler s threshold concentration was 1 in 2 5 millions Ueda (1931, b) found the placental vessels reactive to a smooth muscle stimulant (barium chloride) as early as the fourth month of intra-uterine life, but not reactive to adrenaline (or pilocarpine) before the sixth month From then on the sensitivity to the autonomic drugs increased more rapidly than did that to barium chloride Von Euler found that cocaine sometimes potentiated the adrenaline effect while ergotoxine always abolished it Ergotoxine itself caused a constriction if it was perfused in sufficiently high concentration, this is similar to Budel-

[1] Isolated veins taken from adult animals have reacted to adrenaline in a concentration of 1 in 140 millions (Waterman 1933) and perfused mesenteric veins have contracted at a threshold concentration of 1 in 100 millions (Fleisch 1931)

in the vascular network of the umbilical ring The literature on the small vessels is scattered (Schott, 1836, quoted by Goenner, 1906, Virchow, 1851, quoted by Tait, 1876, Robin, 1860, Tait, 1876, Langer, 1897, quoted by Bondi 1902, Henneberg, 1902, Bondi, 1902, Bucura, 1902, Pfeiffer, 1902, quoted by Kopp, 1937, Goenner, 1906, Jordan 1919, Runge and Hartmann 1927, Kondo, 1930, legend fig 8, Köpp, 1937, Spivack, 1943) and it seems extremely doubtful if any of them can legitimately be styled vasa vasorum (Goenner found openings of venules on the inner surface of the umbilical vein but no corresponding offshoots from the arteries) The profuse distribution of small vessels typical of the pig s cord (Jordan, 1919) and the somewhat similar one in the lamb's cord (Harper, 1943) are not paralleled in the human cord Tait described a sinus, supplied by lower intercostal arteries, in two cords It extended for some distance from the umbilical ring and gave off short branches which Tait considered were nutrient to the matrix, he pointed out that the walls of the sinus were devoid of muscle and that, when it was present, its rupture might lead to continued slight haemorrhage after birth There are no lymphatics in the cord (Schiefferdecker quoted by Köpp, 1937)

(5) *The "valves ' of the umbilical vessels* —These features are said to have been noted by Hoboken (1669) in umbilical arteries, since then "valves" have also been described in the umbilical vein Recent accounts by Shordania (1929, b) Spivack (1936), and Jankovich (1939) are illustrated by photographs (those of Jankovich are particularly telling) and photomicrographs The term valves" is inappropriate from either the structural or the functional point of view (Shordania), Spivack used the term ' folds ' or " constrictions ' in the case of the arteries and " semilunar folds " in the case of the vein for the parts between the folds in the arteries she used the name noduli Hobokenii Jankovich, in respect of the arteries gave as alternatives to 'valves the terms ' folds " and " muscular rings ' So far as the present writers are aware there is no evidence to show that the folds are present before birth, if this is correct then the only interest of the structures is bound up with the part, if any, which they play in the post-natal closures of the vessels To estimate this one must know more about the folds

Shordania said that a single artery contained from 2 to 28 common figures being between 5 and 10, Spivack s maximum was 30, Jankovich gave as an average figure 8 or 9 and as the highest number in his series, 48 Shordania and Spivack both noted that the folds were usually absent from the turns of the spirals and the former on this and other evidence concluded that they cannot be artefacts due to torsion They occur, according to Shordania, mainly in the middle and distal portions of the cord (Jankovich, however, found some within the umbilicus itself) and are ring like projections of the endothelium and media into the lumina of the arteries corresponding indentations are commonly seen on the outer surfaces A fold, according to Spivack may not be equally prominent on both sides of the lumen and may not even, in some cases, completely encircle it The projection consists essentially of a local thickening of both the longitudinal and the circular muscle bundles normally present in the arterial wall, the circular bundles being less mixed than else-



FIG 148 —Human foetus full term Transverse section of umbilical cord Arteries above vein below Note infoldings of surface of cord and absence of small blood vessels (cf *fig 109 f g*) *Scale in mm*

83 cords, all withstood a weight of 4 5 kg, and the average breaking strain was 5 7 kg Rupture occurred most often in the middle third, and not in the proximal third, as found by many earlier workers (Meyer said the placental end was the site of election)

4 *The structure of the cord, the number of its vessels, etc* (fig 148) — Inside an epithelium of one to three, or very rarely of four, layers is the matrix of the cord, which consists of Wharton's jelly with some fine connective tissue bundles, elastic fibres, and stellate and round cells, and which has embedded in it the two umbilical arteries and the umbilical vein,[1] the obliterated remains of the allantois, and *on occasion*, toward the proximal end of the cord, some smaller blood vessels (Shordania, 1929 b) The matrix is anatomically separated from the placental tissues at the one end and the body of the foetus at the other (Tait, 1876) Immediately next to the umbilical vessels there is an increase in the connective tissue fibres of the matrix, and one has to distinguish the vascular wall proper by its greater number of connective tissue fibres and by the presence, in addition, of elastic and smooth muscle fibres

In 95 per cent of cords the umbilical vessels show torsion, according to Shordania, the arteries exhibit it to a greater extent than does the vein (see Morel and Gernez, 1939, fig 2) The same authority gave the following further details The right artery is commonly longer than the left artery, and the latter is longer than the vein The calibre of the vein exceeds those of the arteries, and in 25 per cent of cords the calibre of one artery exceeds that of the other All three vessels decrease in calibre from the placenta to the umbilicus The arteries, in 98 5 per cent of cords, anastomose, the anastomosis is a direct lateral one if it occurs well towards the foetus, but it usually occurs more distally (*in 80 per cent within 2 cm of the placental* insertion of the cord) and is then effected by a cross-vessel of small calibre

The small arterioles and venules often found in the proximal third of the cord were described by Shordania as nutrient vessels of the cord, originating

[1] According to Schultze (1896 156) there may exceptionally be only one artery (as is normal in the mouse) on occasion also there may be two umbilical veins i e a persistence of the condition obtaining earlier in gestation

contracted artery, as noted above, folds can be found projecting into the lumen, they are more numerous in the distal parts, i e where the musculature is less thick Apart from these folds small protuberances are visible in places on the inner surface of the vessel They were called "Polster" by Strawinski who first noted them, and "Buckel by Bondi (1902) They have their greater diameter in the long axis of the vessel, and they occur chiefly at the umbilical end of the cord They are produced by contriction of the inner muscular layer (see below) and, like it, have a somewhat arbitrary distribution The shorter diameter of one pictured by Strawinski (his fig 6) was 0 5 mm and their appearance in such transverse sections explains Kopp's choice of the epithets "mushroom shaped' and "crescentic' According to Bondi (1902), from 1 to 4 may be represented in a cross-section of a contracted artery, and the lumen may thus be crescentic slit like, Y-shaped or X shaped One more general point may be noted before one passes on to the detailed histology, for it can be correlated with the decrease in musculature from the umbilicus to the placenta This point is that, while the cord arteries of the newborn are usually full of blood, one does see a number in which blood is present only towards the placental end (Bondi, 1902)

Descriptions of the histological appearance of the (artificially) dilated artery are very few Pressure dilatation, according to Strawinski does not cause the Polster' to disappear Bondi (1902), on the other hand said that under such treatment the lumen of the vessel becomes approximately cylindrical and that the "valves,' local dilatations and thickenings, and the Buckel" all vanish, in addition, the torsion of the vessel becomes less In such a dilated vessel if one may integrate a number of statements, one can distinguish a single-layered endothelium an elastic muscular inner layer, and a 'circular muscular outer layer (Kopp) The inner layer consists of smooth muscle fibres surrounded by fine elastic fibres The former account for about one fifth of the width of the vessel (Bondi, 1902) and are arranged in spirals with opposite windings (Kopp) The latter appear to be concentrated and to be arranged concentric with the lumen (Bondi) In addition to the above components the inner layer contains some loose connective tissue fibres between the muscle fibres (idem) and also much mucoid (chromotropic) substance which is a precursor of elastic tissue (Kopp) There is a fair amount of support for the idea that the elastic tissue is equivalent to a split up internal elastic lamina (see e g Shallock 1938), and it becomes more like such a lamina where the "longitudinal muscle is absent The outer layer consists predominantly of thick bundles of "circular' muscle fibres, with a respectable amount of very fine elastic and collagen fibres interposed between them the elastic tissue is usually markedly less than that in the inner layer External to the circular musculature there may be bundles of 'longitudinal musculature which in places are not clearly demarcated from the matrix of the cord, hence the external contour of the vessel may show slight irregularities (Köpp) Opinions are divided as to whether or not there is an adventitia Robin (1860) said that its place is taken by Wharton's jelly, Strawinski that it is distinct at the placental end but not at the foetal end, Bucura (1902) that it is poorly developed and scarcely distinguishable from

where with fibres coursing in other directions The dilatations between folds exhibit a corresponding thinning-out of the muscle layers In the present writers' opinion, it seems reasonable to regard the folds as due to extra local reactivity of the arterial musculature, i e as exaggerated local results of the general tendency of that musculature to shorten on exposure to cold, and to the mechanical, thermal, and chemical stimuli (injections with various solutions) that may be involved in the preparation of the cords for examination

According to Shordania, the venous folds are usually long and spiral and unaccompanied by corresponding depressions on the outer aspect of the vessel They occur at the sharp bends and never in the straight parts, and their number in a single vein varies between 1 and 7 Finally, they do not encroach much on the lumen (as the arterial folds commonly do) or offer resistance to perfusion in either direction, and they can be regarded as functionally unimportant Spivack said that the vein possesses semilunar folds, the function of which is not at present known Jankovich gave the average number of folds in a vein as 8 or 9, the maximum in his series was 28 One cannot help thinking that the disproportion between his figures and those of Shordania, for both arteries and veins, lends further support to personal views about the mechanism of production of the folds in both kinds of vessels

(6) *The extra-abdominal portions of the umbilical arteries* —The following account should be integrated with the description of the intra-abdominal portions of these vessels (see section xiii below), if readers wish to get an idea of the umbilical arteries as a whole The present arrangement has been adopted in order that they may get an idea of the umbilical cord as a whole

It is not easy to give a concise account of the cord arteries In the first place, there are differences between individual arteries, between the different parts of a single artery, and even between opposite sides of a single transverse section Secondly, the great muscularity and reactivity of the vessels makes it difficult to fix them in their naturally dilated state, hence all but a few histological accounts refer to contracted or partially contracted specimens Finally, no one has seriously attempted to bridge the gap between macroscopic appearances and histological findings, either by dissection under slight magnification or by reconstruction from serial sections Hence one has no complete guide to the essential structural plan of the vessels, and the best that one can offer is the description, as yet unconfirmed by other workers, that was given by von Hayek (1935) Cineradiographic studies of the placental circulation from the birth of the child onwards would supply many of the details at present missing from the functional anatomical picture

The extra-abdominal portions of the arteries are softer, looser in structure, and paler than the intra-abdominal ones (Strawinski, 1875) The width of their musculature rises rather rapidly to a maximum just inside the umbilical ring, at the proximal end of the cord it is about two-thirds of this maximum, and thereafter it gradually decreases until at the distal end it is about one-third of the maximum (idem) It is more powerful than that of the extra-abdominal vein, for post-natally contracted arteries cannot for some hours be dilated by pressure, whereas the vein can (Strawinski, Shordania, 1929, b) In a

the lumen Were the inner fibres circularly disposed, they would have to contract to a seventh or less of their original length to cause such obliteration, and so far as is known no smooth muscle can shorten to this extent Further, contracted circular muscle could not produce a lumen star shaped in transverse section For further details about the musculature, and for an account of the disposition of the collagen fibres, the reader should consult von Hayek's paper Like the ductus arteriosus, the umbilical arteries are prepared during development for a single post natal performance and are allowed no rehearsals for it

(7) *The extra abdominal portion of the umbilical vein* —The vein is thinner-walled than the arteries but much thicker-walled than any other veins of similar calibre Its lumen in the dilated state is round or oval (Bondi, 1902), in the contracted state also it is usually circular, i e there are no protuberances into the lumen, as there are in the case of the arteries

There is a single layered endothelium, and external to it a well marked internal elastic membrane, which in places may be split up into layers, and which according to Shordania (1929 b) becomes stronger towards the foetal end of the vessel The media lies external to the membrane and consists of bundles of smooth muscle with large spaces between them These spaces are greater than the corresponding ones in the arterial walls and the loose interstitial tissue in them makes for great distensibility of the vein About the disposition of the muscle bundles there are conflicting statements The inner layer when present is "longitudinal", on occasion it is wide (Kopp, 1937) but in other cases it is poorly developed or absent (Runge and Hartmann 1927 Shordania 1929, b) The middle layer is regarded by most writers as the most constant and the largest, it is usually "circular" but its fibres and those of the outer 'longitudinal' layer may be interwoven in the middle portion of the cord (Shordania, 1929, b) The outer layer is thicker than the 'circular' layer according to Shordania In general, views about the muscular arrangements are as various in more recent literature as they were in the literature available to Henneberg (1902), and they must be regarded as indications of considerable variability in the structural plan of the vein Wharton's jelly is a substitute for an adventitia over most of the vein's length, and the vessel is separable from it with greater difficulty than are the arteries (Runge Baur and Hartmann, 1928) Mucoid tissue is less in amount in the vein (Kopp) According to Bondi (1905), the structure of the vessel changes fairly abruptly to the intra abdominal type either in the proximal part of the cord or near the umbilical ring, and a connective tissue sheath is present round the vein before it reaches the umbilicus, though more distally there is no adventitia Elastic tissue is less (Strawinski, 1875) or markedly less (Kondo 1930) in the vein than in the arteries, and it is practically limited to the inner half of the wall (Jordan 1919)

(8) *The attachments of the cord vessels* —Tait (1876) said that the cord matrix ends proximally in three cone like processes and that in the umbilical ring nothing of the cord is found except the three umbilical vessels Bondi (1905), on the other hand, stated that the umbilical arteries are ensheathed, for 1 to 2 cm proximal to the cord, in Wharton's jelly plus a variable amount

the cord matrix, and Morel and Gernez (1939) much the same Shordania (1929, b) stated that the adventitia of the arteries is more marked than that of the vein, Kopp (1937) and Spivack (1943) that there is no adventitia Runge, Baur and Hartmann (1928) found that the arteries are more easily separated from the matrix of the cord than is the vein

In the contracted artery there may be complete disappearance of the vascular lumen, with only a dot, or a crescentic, slit-like, Y- or X-shaped line to mark its place The dot will be present where " longitudinal " muscle is absent, the other shapes will result from projection into the lumen of 1 to 4 " Polster " of " longitudinal " muscle, which has contracted simultaneously with the outer " circular " muscle The retraction and contraction of the musculature is made possible by the presence of loose connective tissue between the fibres and bundles If contraction of the outer musculature is not everywhere equal, " folds " of Hoboken may appear and partially or completely subdivide the vascular lumen into segments, so that it resembles a string of miniature sausages (Jankovich, 1939) One need not pursue farther the possible variations in the macroscopic or microscopic picture, for they are legion, details can be found in the papers already quoted and in others not yet specifically mentioned (e g Hofmann, 1877, Henneberg, 1902, Bucura, 1902, Jordan, 1919, Kondo, 1930, Popoff, 1938)

It is, however, necessary to give some longer account of the complex spiral arrangement of the musculature, as conceived by von Hayek (other suggestions that the musculature is spirally arranged occur in Tait, 1876, Hofmann, 1877, Bondi, 1902, and Kopp, 1937) The material which von Hayek examined consisted of uncontracted and contracted vessels from newborn, full-term infants He found that, when an artery contracts, its external calibre falls to a half or a third of its original value, the wall increases three or four times in thickness, and the wide circular lumen is reduced to an impervious slit, star-shaped in transverse section There are two coats of muscle in the arterial wall Each is made up of helicoid spirals with opposite windings [1] The pitch of the spirals is less in the outer coat than in the inner one, so the former approximates more to circular muscle and the latter to longitudinal muscle In the uncontracted state of the artery, the outer coat appears to be circularly arranged or nearly so, in the contracted state the inner coat appears more longitudinal and the outer less circular There is no sharp division between the two coats and fibres pass from one to the other When a particular helicoid spiral is getting near the end of its winding-up process, the fibres in it approach the lumen of the vessel and perhaps end in relation to the well-developed internal elastic membrane The star-shaped appearance of the inside of the contracted artery, as seen in transverse sections, may result from asynchronous contraction of different muscle bundles The result of the helicoid arrangement of the muscle fibres is that a relatively small contraction (a shortening of about 50 per cent) can bring about complete obliteration of

[1] Von Hayek distinguished between a simple *spiral* (Spirale) in a single plane (e g a watch spring) a *helicoid spiral* (Schneckenlinie) such as would be produced if one raised the centre of the watch spring or such as occurs naturally in the snail shell and a *screw spiral* (Schraubenlinie) in which the spiral remains at a fixed distance from its axis and has a constant pitch (as e g in a screw used for metalwork or in a circular staircase)

drug had to be used in higher concentrations than was necessary with other arteries in order to produce a contraction and it was therefore concluded that the effect was a muscular rather than a neuro-muscular one Parasympathetic stimulants and depressants produced little or no response, histamine caused contraction and barium chloride was effective in concentrations as low as 1 in 100,000 Waterman (1933) reviewed past work upon the umbilical vein and also reported personal findings Except for Kusnetzow and Norizin (1929, 1930) all previous observers had reported little or no reaction to adrenaline Waterman himself usually found contraction but only with concentrations about a thousand times as high as were required for other veins Previous workers and Waterman likewise, were unable to discover any or any marked, reactions to parasympathetic drugs, the response to pituitrin was a contraction in some cases, in others nil

(iii) THE INTRA ABDOMINAL PORTION OF THE UMBILICAL VEIN

This vessel runs partly enfolded by peritoneum and is surrounded, in well developed infants by subserous fat (Bondi 1905), it is accompanied by lymph vessels which arise from the umbilical ring and the wall of the vein near that ring and then pass to the porta hepatis (Enomoto, 1930) Within 2 or 3 cm from the ring it has undergone a complete change of structure (Strawinski 1875 Runge and Hartmann 1927) and is slack and collapsible by comparison with the extra abdominal portion (Hofmann, 1877) It exhibits no valves or spirals (Bondi 1905)

The internal elastic membrane is poorly developed or, especially towards the liver completely absent Thick connective tissue, including some fine elastic fibrils lies between the intima and the musculature of the media The muscle does not form a continuous layer but is in bundles separated by compact connective tissue which often especially towards the liver, predominates over the contractile tissue There are conflicting views about the direction of the muscle fibres Henneberg (1902) stated that the inner fibres were chiefly longitudinal and were more numerous than the circular ones Runge and Hartmann wrote that there was a small thin layer of circular fibres directly outside the intima and apart from that only a few scattered fibres here and there in the firm connective tissue The adventitia, according to Bondi is the largest part of the vessel Rich fairly thick, fibrillar tissue encloses numerous mostly longitudinal muscle bundles, the elastic fibres are plentiful and are disposed in membranes and nets of various thicknesses, finally many vasa vasis and nerve fibres are present According to Schott (1836 quoted by Goenner 1906 and others), the nerves to the vein are from 5 to 7 in number, they arise from the left hepatic plexus and pass down on the dorsal surface of the vein anastomosing with one another en route (see also Spivack, 1943)

Summarizing one may say that, after the sudden gross change in structure near the umbilicus the vein tends to have less muscular tissue, and more connective tissue, the nearer it gets to the liver (Bondi, 1905) The internal elastic lamina fades out during the same course (idem, 1902), and the adventitia

of connective tissue The sheath so formed is closely connected by tense connective tissue both to the umbilical ring and also to the local fascia (Sachs' fascia umbilicalis), which is often very markedly developed, more proximally the sheath passes over into the adventitia of the intra-abdominal portions of the arteries Within the sheath, as in the cord jelly proper, the arteries are freely movable and they are only indirectly connected with the abdominal wall—a fact of importance for the understanding of their post-natal retraction The picture in the case of the vein is somewhat different The vessel develops an adventitia in the proximal portion of the cord, and at the umbilical ring it is attached fairly firmly to the skin, but comparatively loosely to the fascia Meyer (1914, a, b) contrasted the firm attachments of the human arteries and the vein to the umbilical ring with the loose attachments of the arteries of ruminants He also thought that the consistence of the cord matrix in the human subject was such as to hinder post-natal retraction of the divided vessels towards the umbilicus Kopp (1937) said that the vessels are more closely attached to the surrounding tissue in the proximal 6 cm or so of the cord than in its more distal portion

(9) *The innervation, reactivity, and pharmacology of the cord vessels* — Spivack (1943) produced so complete a review of past work [1] upon the innervation and made so careful and critical a personal study, that there is no need to duplicate her account here Her conclusion is that "modern neuro histological methods appear to show that the umbilical blood vessels of the cord proper in man are devoid of a nervous apparatus"

The reactivity of the vessels is such as one would expect in view of their great muscularity and the absence of a nerve supply to them A resume of earlier work upon them was given by Schmitt (1922), and from it one may quote the note about some experiments performed by Bucura (1907) Circumscribed spots on the cord were stimulated electrically immediately after the birth of the child, and the vessels at once contracted down completely at these points, while elsewhere they remained full of blood Division of the cord at the sites of contraction resulted in no haemorrhage, but division 1 cm on either side of these sites was followed by haemorrhage, i e the reaction to the electrical stimulation was sharply localized and not propagated

Rech (1925) paralleled upon isolated lengths of cord arteries the perfusion experiments carried out earlier (1922, 1923) by Schmitt upon placental vessels Like Schmitt, he reported intense reactivity to the presence of oxygen in the perfusion solutions, the contractions induced by saturated solutions were so strong that the vessels would not reopen under considerable pressure On the other hand, perfusion with carbon dioxide or nitrogen saturated solutions resulted in dilatation of the vessels Baur, Runge and Hartmann (1929) confirmed the reactivity of the umbilical arteries to oxygen, but found little effect upon the vein, potassium cyanide abolished the arterial reaction to oxygen

The same workers studied the pharmacology of the arteries both in perfusion experiments and also in experiments upon isolated preparations The vessels were equally reactive to adrenaline throughout their length, but the

[1] Baur Runge and Hartmann (1929) might perhaps be added to her list of references

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(iii) THE INTRA ABDOMINAL PORTION OF THE UMBILICAL VEIN

This vessel runs partly enfolded by peritoneum and is surrounded in well-developed infants by subserous fat (Bondi, 1905), it is accompanied by lymph vessels which arise from the umbilical ring and the wall of the vein near that ring, and then pass to the porta hepatis (Enomoto, 1930) Within 2 or 3 cm from the ring it has undergone a complete change of structure (Strawinski, 1875, Runge and Hartmann 1927) and is slack and collapsible by comparison with the extra abdominal portion (Hofmann, 1877) It exhibits no "valves" or spirals (Bondi, 1905)

The internal elastic membrane is poorly developed or, especially towards the liver, completely absent Thick connective tissue including some fine elastic fibrils lies between the intima and the musculature of the media The muscle does not form a continuous layer but is in bundles separated by compact connective tissue, which often especially towards the liver, predominates over the contractile tissue There are conflicting views about the direction of the muscle fibres Henneberg (1902) stated that the inner fibres were chiefly longitudinal and were more numerous than the circular ones Runge and Hartmann wrote that there was a small thin layer of circular fibres directly outside the intima and apart from that only a few scattered fibres here and there in the firm connective tissue The adventitia, according to Bondi is the largest part of the vessel Rich fairly thick, fibrillar tissue encloses numerous, mostly longitudinal muscle bundles, the elastic fibres are plentiful and are disposed in membranes and nets of various thicknesses, finally many vasa vasis and nerve fibres are present According to Schott (1836 quoted by Goenner, 1906 and others) the nerves to the vein are from 3 to 7 in number, they arise from the left hepatic plexus and pass down on the dorsal surface of the vein anastomosing with one another en route (see also Spivack 1943)

Summarizing one may say that, after the sudden gross change in structure near the umbilicus the vein tends to have less muscular tissue and more connective tissue the nearer it gets to the liver (Bondi 1905) The internal elastic lamina fades out during the same course (idem, 1902), and the adventitia

appears to increase in thickness But these are generalizations to which exceptions are fairly frequent (idem, 1905) The longitudinal musculature presumably plays a part in the delayed post partum retraction of the umbilical vein away from the umbilical ring (Robin, 1860, Baumgarten, 1877, Meyer, 1914, a, b, and others), but that forms no part of the story that is to be told in this book

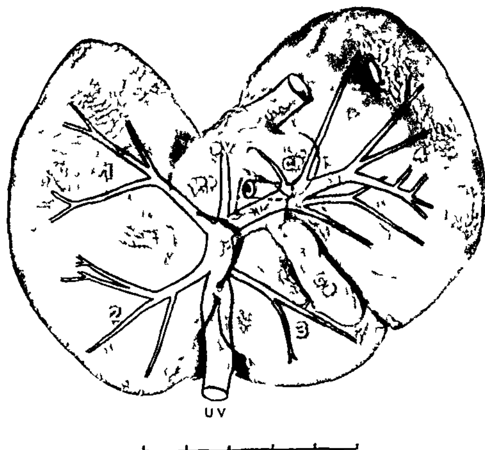


FIG 149 —Human foetus 38 weeks Caudal view of liver to show afferent venous distribution ascertained by dissection *PP* papillary process *CP* caudate process *GB* gall bladder *UV* umbilical vein giving offshoots to *3* central mass right *2* central mass left and *1* left mass *DV* ductus venosus *SI* sinus intermedius *PV* portal vein giving offshoots to *4* right mass *IVC* inferior vena cava Scale in cm

(iv) THE LIVER AND THE DUCTUS VENOSUS

The proportion of the body weight that is provided by the liver weight is, according to Needham (1931, 451), at its maximum, 7 5 per cent, at 2 5 months and has fallen to 5 0 per cent by birth In the adult, according to Piersol, it is about 2 5 per cent The papillary and caudate processes are of proportionately greater size in the foetus than in the adult (Thomson, 1899)

Fig 149 shows the afferent venous pattern (ascertained by dissection) superimposed upon a photograph of the caudal aspect of the liver from a 38-weeks' foetus From this figure it is apparent that the viscus is divisible, according to the schema given in Chapter VII, into left mass, central mass left, central mass right, right mass, and papillary and caudate processes, the

mid line of the umbilical vein being a guide to the partition of the central mass. The anatomical portal moiety furnishes a larger proportion of the total liver weight in the human foetus than it does in the lamb. The gall bladder is disposed somewhat across the division between the central and right masses. The papillary and caudate processes are small. The extra hepatic portion of the umbilical vein may be contracted down, either partially or almost completely.

The hepatic venous collection is in general accord with the schema in Chapter VII. Thus, one main trunk drains the left mass and central mass left, a second drains the central mass right and a third drains the right mass, though the tributaries of the second vessel may in some measure invade the particular territory of the third.

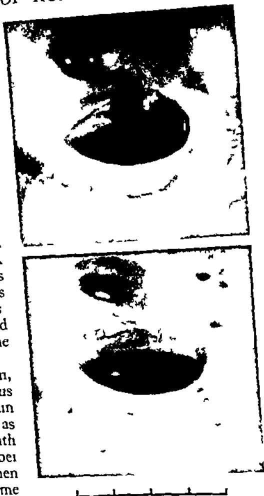


FIG. 150.—Human foetus, age unknown. Two views of the opening (that shown in the centre of each photograph) leading from the umbilical vein into the ductus venosus. The views are such as one gets by opening up the umbilical vein in a fresh liver and then looking at the caudal aspect in a mirror held below the viscus. Scale in mm.

'Lipping', i.e. a sphincter mechanism, is present at the beginning of the ductus venosus (figs. 150, 151); this may explain Ziegenspeck's (1905) finding that it was difficult to inject the channel after death ("Oft geht der Duktus gar nicht auf bei der Injektion, während andere Venen und der Sinus aufgehen"). The same author considered the ductus a stationary vessel both anatomically and physiologically from the 16th to the 20th week of foetal life onwards. If his view is correct then Man would appear to be intermediate in respect of the ductus venosus between the sheep, in which the channel increases in size and remains functional up to the time of birth, and the horse, in which it is non existent at birth. So far as a short series of personal findings allows one to say, the ductus in Man is fairly short (e.g. it was 1.6 cm. long in two practically full term foetuses) and fairly straight; it remains of approximately the same width, or broadens gradually, as it passes to its termination. Schneider (1937) gives some references to literature on anomalies of the channel.

The inferior vena cava is not a very wide vessel at its entry into the liver, and the accessory hepatic veins which it receives before it unites with the right hepatic vein are too small to cause any significant increase in the calibre of the trunk.

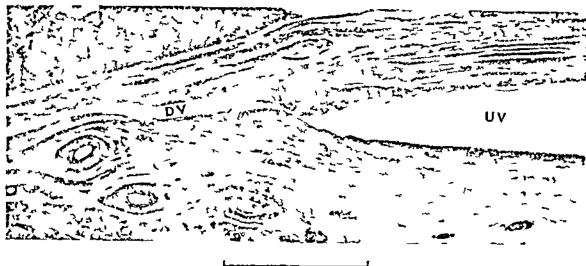


FIG 151.—Human foetus stillborn Longitudinal section (top of fig cranial bottom caudal) across junction of umbilical vein *U V* and ductus venosus *D V* to show smooth muscle sphincter closing the entry from the former into the latter Note the nerve just above the sphincter and the vascularity of the tissue below and to the left of it Scale 1 mm

(v) THE INFERIOR CAVAL CHANNEL AND ITS TERMINAL BIFURCATION

In Man the inferior caval channel is very short At its beginning, i e after the inferior vena cava has united with the hepatic veins and the ductus venosus, it is very much wider than the abdominal vena cava, e g it was well over twice as wide in one practically full-term foetus This increase in calibre is not usually shown in diagrams of the foetal cardiovascular system

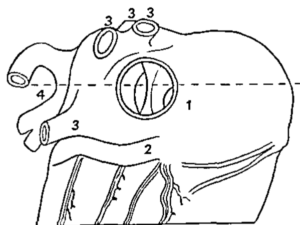


FIG 152.—Newborn child 54 cm long Outline drawing from fig 1 in Ziegenspeck (1905) showing caudal view of part of heart etc The interrupted line shows the line of section for the production of fig 153 Original legend *1* inferior vena cava with limbus Vieussenii [crista dividens] and valve of foramen ovale [free or apposable portion of via sinistra] *2* coronary sinus *3 3 3* pulmonary veins *4* pulmonary artery and ductus arteriosus

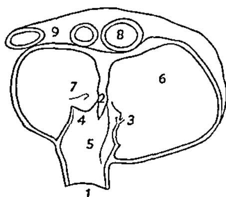


FIG 153.—Same subject as in fig 152 Outline drawing from fig 2 in Ziegenspeck (1905) showing view towards apex of heart revealed by cut along interrupted line in fig 152 Original legend *1* inferior vena cava [inferior caval channel] *2* septum atriorum and limbus Vieussenii [crista dividens] *3* Eustachian valve [free portion of via dextra] *4* valve of foramen ovale [free or apposable portion of via sinistra] *5* recess remains of sinus venosus *6* right ostium venosum *7* left ostium venosum *8* bulbus arteriosus *9* pulmonary artery

Within the heart the channel bifurcates, on a well marked crista dividens (figs 152–154) into left and right terminal divisions, or viae sinistra et dextra To expose the crista dividens, one needs only to remove the inferior vena cava completely, as in the case depicted in fig 154 in doing so, one must be careful not to cut the pars libera viae dextrae ("Eustachian valve") which if large and somewhat slack may have prolapsed back to some extent, post mortem into the vena cava The view has previously been expressed (e g by Retzius 1835) that the inferior caval channel inclines somewhat to the left, personal findings are not available because it has not been possible from a limited number of specimens, to devote a series to settling this particular point Ziegenspeck, to whose accounts (1884 1905) the reader is specially referred, took great care in the fixation of his specimens, and he certainly showed a leftward inclination of the inferior caval channel in his figure (fig 153 of the present book) It is also apparent in fig 1 (fig 155 of the present book) of the paper by Keen (1942)

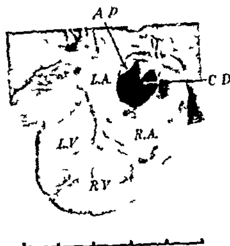


FIG 154—Human foetus 8½ months Caudal view of heart and part of lungs to show crista dividens C D or dividing ridge of inferior caval channel Inferior vena cava itself entirely removed R A L A right and left atria R V L V right and left ventricles A P part of free or apposable portion of via sinistra Scale in cm

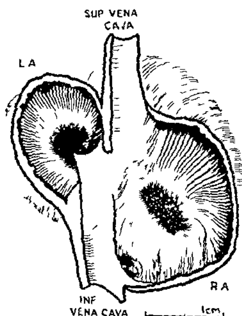


FIG 153—Human foetus ? 8 weeks From Keen (1942) View towards apex of heart after removal of parts of right and left atria R A L A etc *Inf vena cava sup vena cava* inferior and upper caval channels Via sinistra fully open

(vi) THE VIA SINISTRA AND ITS PARS LIBERA

The "foramen ovale" and its "valve" and the post natal closure of the channel have been the subject of many publications, among which one may mention particularly those of Ziegenspeck of Patten and his colleagues and of Keen (1942) The figure given by Patten (1931, 27) of the interior of the left atrium at birth is a specially useful one, for this view is one that is seldom portrayed in books Keen's figures are very clear and instructive and well worth attention

The via sinistra is relatively shorter in the human subject than in foetuses of many lower animals, and the pars

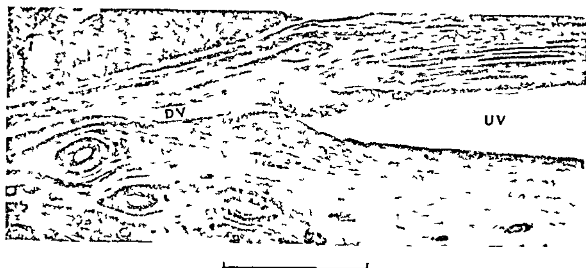


FIG 151 —Human foetus stillborn Longitudinal section (top of fig cranial bottom caudal) across junction of umbilical vein *UV* and ductus venosus *DV* to show *smooth muscle sphincter closing the* entry from the former into the latter Note the nerve just above the sphincter and the vascularity of the tissue below and to the left of it Scale 1 mm

(v) THE INFERIOR CAVAL CHANNEL AND ITS TERMINAL BIFURCATION

In Man the inferior caval channel is very short At its beginning, i e after the inferior vena cava has united with the hepatic veins and the ductus venosus, it is very much wider than the abdominal vena cava, e g it was well over twice as wide in one practically full-term foetus This increase in calibre is not usually shown in diagrams of the foetal cardiovascular system

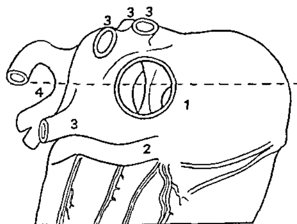


FIG 152 —Newborn child 54 cm long Outline drawing from fig 1 in Ziegenspeck (1905) showing caudal view of part of heart etc The interrupted line shows the line of section for the production of fig 153 Original legend *1* inferior vena cava with limbus Vieussenii [crista dividens] and valve of foramen ovale [free or apposable portion of via sinistra] *2* coronary sinus *3 3 3* pulmonary veins *4* pulmonary artery and ductus arteriosus

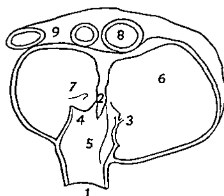


FIG 153 —*Same subject as in fig 152* Outline drawing from fig 2 in Ziegenspeck (1905) showing view towards apex of heart revealed by cut along interrupted line in fig 152 Original legend *1* inferior vena cava [inferior caval channel] *2* septum atriorum and limbus Vieussenii [crista dividens] *3* Eustachian valve [free portion of via dextra] *4* valve of foramen ovale [free or apposable portion of via sinistra] *5* recess remains of sinus venosus *6* right ostium venosum *7* left ostium venosum *8* bulbus arteriosus *9* pulmonary artery

FIG 157—Human foetus stillborn (not the same one as in fig 156) Right and left lateral sternal dorsal and caudal views of thoracic viscera to show lobation of lungs (cf figs 158 159) lie of heart etc (*Note* the ductus arteriosus *D A* is abnormal) *R 1 R* incompletely separate right apical and cardiac lobes *R 3* right diaphragmatic lobe *L 1 L* fused left apical and cardiac lobes *I C C* *S C C* inferior and superior caval channels *R A* right atrium *R V* *L V* right and left ventricles *P T* pulmonary trunk A aorta *I A* *L C C A* *L S A* innominate left common carotid and left subclavian arteries *Tr* trachea *O* oesophagus *Az* azygos vein Scale in cm

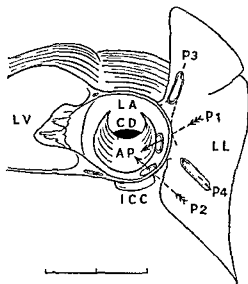


FIG 156—Human foetus stillborn Semi diagrammatic drawing of dissection of heart to show the free or apposable portion *AP* of the via sinistra and its intimate relation to the opening of *P 1* the right cranial pulmonary vein Parts of the left ventricle *LV* left atrium *LA* and left lung *LL* removed *ICC* inferior caval channel *CD* crista dividens or dividing ridge *P 2 right caudal pulmonary vein P 3 left* cranial pulmonary vein *P 4* left caudal pulmonary vein The arrows indicate approximate directions of blood streams *of P 1 and P 2* Scale *in cm*

libera is of the simple primate-carnivore type, it is rather diagrammatically pictured in fig 156 Personal findings are that the cornua of the pars libera may be at more or less the same level, or the dorsal one may be somewhat more cranial than the sternal one *The free border varies in its* depth of curve according to the positions of the cornua and the degree of slackness of the membrane itself The relative length of the pars libera is variable from specimen to specimen Towards term the musculature in the membrane is very apparent, and presumably it contracts and relaxes at cardiac rate, as it has been shown to do in the lamb The pars libera is in special relation to the entry of the pulmonary venous drainage from the upper two lobes of the right lung (see section x below)

(vii) THE VIA DEXTRA AND ITS PARS LIBERA

In Man the presence of a pars libera viae dextrae (the "Eustachian valve") makes for a more precise definition of the termination of the via dextra For the free border of the "valve" is obviously one limit and the crista interveniens another *It is generally accepted that the* membrane is not fenestrated before birth, on the other hand, its degree of development varies from foetus to foetus (cf Keen, 1942, 108) About its function there are many hypotheses, but none of them is supported by any satisfactory evidence One that has been popular for about two centuries is that the membrane directs the inferior caval stream towards the "foramen ovale" If it does ever do so, it can only be because of a rise of pressure in the right atrium, and such a rise of pressure could effect the same result without the membrane being present *Actually, any directing of the inferior caval* stream to the left is more likely to result from the inclination of the inferior caval channel itself

(viii) THE CORONARY SINUS AND THE THEBESIAN VALVE

In the normal human heart the coronary sinus is the channel for the cardiac venous return only, it does not, in addition, carry the larger part of the azygos venous return, as *in the lamb and similar animals* In a series of 100 post-natal subjects, Gruber (1864) found the Thebesian valve well developed in 88, rudimentary in 7, and wanting in 5 Its function is a matter of surmise

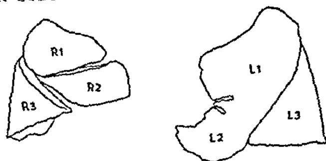


FIG 159 — Newborn baby Outline drawings of lungs from Blechschmidt (1935) *figs 6 and 5* The right lung is almost completely separated into apical *R 1* cardiac *R 2* and diaphragmatic *R 3* lobes In the left lung there is fair separation of the apical *L 1* and cardiac *L* lobes the diaphragmatic lobe *L 3* appears to be completely separate or nearly so

associable with the extreme shortness of the thoracic inferior vena cava The three lobes are largely separate, in one specimen almost completely so (fig 158) On the left side there is more or less complete fusion between what would be the apical and cardiac lobes of lower animals, but it is not unusual to get partial indication of the limits of the two masses (see, e g, figs 158, 159) The left apical cum-cardiac portion is more or less well separated from the part corresponding to the diaphragmatic lobe of lower animals

There are four pulmonary vein entries namely right and left cranial and caudal (fig 155) The right cranial entry is for the veins draining the right apical and cardiac lobes, the right and left caudal entries for the veins draining the right and left diaphragmatic lobes respectively, and the left cranial entry for the veins draining the more or less fused left cardiac and apical lobes The right cranial entry is in close relation to the pars libera viae sinistrae, i e the human foetus is similar in this respect to other foetuses (Franklin, Amoroso Barclay and Prichard, 1942)

(xi) THE SUPERIOR CAVAL CHANNEL AND ITS RELATION TO THE VIA DEXTRA, THE CRISTA INTERVENIENS

Exceptionally in Man the superior caval channel may be in duplicate through arrest of the normal development of this part of the venous system A human foetus possessed in this way, of right and left channels was described by Harris (1922 a) who said that the Thebesian valve, at the opening of the left channel was larger than normal[1] More exceptional than bilateral superior venae cavae is a superior caval valve such as was described by Turner (1868–9)

When there are two superior caval channels, it is the right one that is in relation to the via dextra and the terminal part of the left one replaces the coronary sinus In the more normal subject the junction of the single superior caval channel and the via dextra is the crista interveniens One cannot give here all the conflicting views that have been published since Lower in 1669 first described his ' tubercle,' but one may mention a

[1] Thus providing an exception to the generalization (In the cases I have examined the persistence of a left superior vena cava is always accompanied by absence of a Thebesian valve) that he made later in the same year (Harris 19 2 b) Actually Gruber (1864 65 see also his Pl II fig 2) had long before noted the presence of the valve *in some* post natal cases of bilateral superior venae cavae

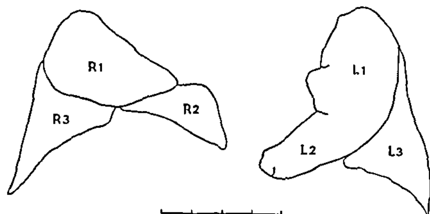


FIG 158—Human foetus stillborn (same one as in fig 156) Right and left lateral views of lungs There is much greater separation than in the last specimen (fig 157) of the right apical *R1* and right cardiac *R 2* lobes Other lettering as in fig 157 Scale in cm

(ix) THE HEART

The human being is one of a relatively small number of mammals in which the apex of the heart lies well to the left of the sternal mid line (fig 157), both ventricles may be concerned in its formation, though this is more commonly ascribed to the left ventricle alone[1] In a series of foetal and immediately post-natal hearts, Keen (1942) found that the ventricles took an equal share in forming the apex and were alike in the thickness of their muscle walls in cross sections (see his fig 5), made half-way between the atrio-ventricular groove and the apex, and also nearer the apex "Most observers," he wrote, "are agreed that the capacities of the two ventricles in the foetal mammal are the same and that the right and left ventricles maintain equal pressures and expel equal quantities of blood" Actually, the only part of this statement that has been proved for the normal foetus is the equality of pressures, which was demonstrated by Hamilton, Woodbury and Woods (1937) in dogs and rabbits, indirect evidence is present in the Nuffield Institute records of foetal lambs, for contrast medium does not pass into the first part of the aorta from the patent ductus arteriosus, or vice versa One can scarcely accept Pohlman's measurements of the capacities of the foetal pig's ventricles, as Keen does, unless one is prepared also to accept the rest of Pohlman's work on the same animals Finally, there is no direct evidence available as to the outputs of the two ventricles in the foetus It may be possible to obtain such evidence by the use of Thermostromuhrs but, until it is so obtained, opinions should continue to be distinguished from facts

(x) THE LOBATION OF THE LUNGS THE PULMONARY VEINS AND THE RELATIONS OF THEIR OPENINGS TO THE VIA SINISTRA (figs 156–159)

In all the specimens personally examined there are three lobes on the right side, absence of the intermediate lobe of lower animals being, presumably,

[1] An exceptional case in which the apex was bifid (as it normally is in the dugong see Home 1823 III 169 IV Tab L Carus and Otto 1843 fig III) was described by Thomas Bartholin (1654 Cent I Hist LXVII pp 117–18) Christophorus Gióe he wrote narravit mihi in Norwegia pridem à se visum latronem qui pœnas scelerum luebat Quum extentaretur à carnifice cor habuisse singularis figura mucrone non acuto ut fieri solet sed bifido ut distincti ventriculi manifestius externa facie apparuerint dexter nempe & sinister interjecto hiatu Later cases are referred to by Walmsley (1929 2–)

(xii) THE PULMONARY TRUNK, DUCTUS ARTERIOSUS, AND AORTA

The vast literature upon the ductus arteriosus and the vessels which it joins will not be quoted at any length, references can be found in the papers specifically mentioned It should be remembered that anatomical statements may require modification here and there if, at some future date, cineradiographic studies become possible in the human infant [1]

For the macroscopical details one can consult Noback and Rehman (1941) and, in respect of a particular point, Jager and Wollenman (1942, 599) The large calibre of the ductus was noted by Jean Mery and others over two centuries ago, Noback and Rehman said that it was equal to, or greater than, that of the pulmonary artery, aortic arch, or descending aorta In 93 per cent of Jager and Wollenman s specimens the channel was cylindrical in cross section Its course is best understood by reference to Noback and Rehman s fig 12 if one adds their note that the channel bulges markedly to the left (this bulge is not of course, seen in the fig) it unites with the aorta sterno laterally about 1 cm distal to the origin of the left subclavian artery Strassmann (1894) claimed that the "party-wall' at the union of the two vessels acts as a sort of valve and closes the ductus when the aortic pressure rises after birth Wells (1908) and Swensson (1939) mentioned some of the earlier support and opposition accorded, after 1894 to Strassmann s concept Hamilton, Woodbury and Woods (1937) who considered that the ductus arteriosus was functionally closed in the rabbit and dog by such a 'valve,' admitted its absence in the human subject Noback and Rehman said it does not exist, but they reported the presence of a transverse ridge, situated about half-way between the pulmonary and aortic ends of the ductus, in about 25 per cent of their specimens The ridge is depicted in their fig 12 it lies on the caudal aspect of the channel and according to Noback and Rehman (519) may occlude as much as half of the lumen One would particularly like to determine by means of cineradiography, if the ridge is present in the living state Apart from this feature (which is stated to be present in only 1 in 4 specimens), one may say that the macroscopic appearance of the ductus in mature human foetuses is very similar to that found in a wide range of animals personally studied, indeed, the main point in which differences occur between genera would appear to be the acuteness of the angle at which the ductus and aorta unite and this divergence is not, one would imagine, a matter of any great significance

According to Swensson (1939) Langer (1857) was the first to recognize the histological differences between the ductus arteriosus and the vessels which it unites More recently, it has become customary to speak of the ductus as a typically muscular artery, and of the pulmonary trunk and aorta as typically elastic arteries (see e g Costa, 1930) Accounts of the microscopical structure agree in some points and disagree in others the disagreement may be due to individual variations between specimens (Jager and Wollenman 1942) or to the different levels of section The account which

[1] Radiographic studies of the patent ductus arteriosus have recently been described by Donovan et al 1939 and by Steinberg et al 1939

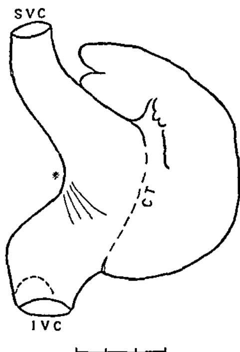


FIG 160—Human subject Outline drawing from Tandler (1913) fig 32 Corrosion preparation of right atrium etc the injection was made with the pericardium intact in order to preserve the true form of the crista interveniens * (tubercle or torus of Lower) *I V C S V C* inferior and superior venae cavae *C T* line of crista terminalis Lower interrupted line opening of tributary vein into *I V C* Scale in cm

few of the more recent ones Tandler (1913) pointed out that neither in the foetus nor in the adult do the axes of the venae cavae form a straight line, but they bend sternally to form a blunt angle at their meeting point (fig 160), the angle disappears if one opens the pericardium carelessly The tubercle is not, however, merely the angle between the venae cavae but also the site of a more or less strongly developed, transverse bundle of muscle fibres, the fasciculus Loweri, the adipose tissue, described by Henle, is also visible both macro- and microscopically Walmsley (1929) recognized the existence of the swelling but noted that it is much less strongly developed in Man than in pronograde animals The angle of junction, he said, is about 140° in Man and the anthropoids, in many other mammals, and in the human foetus, it is about 100°

Personal findings have been as follows The crista interveniens is definitely not so prominent in the human foetus as in those of many lower animals, and part of the bulge seems to be due, at least in some cases, to an underlying pulmonary vein (the one draining the right apical and cardiac lobes)[1], a similar finding has been made in some other species Viewed from the cranial aspect the edge of the crista is seen to be curved, with its concavity facing well over to the right of the sternal mid-line One imagines that the superior caval blood is directed somewhat sternally and somewhat to the right by the disposition of the superior caval channel as a whole Because the apex of the human heart is well to the left of the sternum and the crista interveniens faces somewhat to the right, this ridge and the crista dividens are much more in line (viewed from the cranial aspect) than the corresponding structures in many other foetuses, there is, however, no need to confuse the two, as some writers appear to do

This note about the crista interveniens is purposely brief, for personal findings are as yet too few for any fuller statement One hopes that it may be possible, at some future date, to produce a more extended account of the ridge and of its anatomical and functional relations to other structures At present one can certainly not pretend to have settled all the disputes of nearly three centuries

[1] This recalls Cheselden (1713 114) In the right [Auricle] at the meeting of the Cava s is an Eminence call d Tuberculum Loweri this is chiefly rais d by the succumbent Pulmonary Artery and Vein

the intima Von Hayek (1935) attempted to go beyond mere sections in various planes, and to produce a picture of the musculature of the vessel as a whole External to the internal elastic membrane, he said, are two coats of smooth muscle, in both the fibres form sets of helicoid spirals (see footnotes in section ii above) with opposite windings, the pitch of the spirals is less in the outer layer which therefore approximates more to a circular musculature, and greater in the inner layer, which therefore approximates more to a longitudinal musculature In the dilated ductus the approximation to circular is increased, in the contracted ductus that to longitudinal The result of the helicoid arrangement is that the muscle fibres need not shorten excessively in order to produce obliteration of the lumen (see the explanatory diagrams in the first part of von Hayek's paper) The pulmonary trunk, ductus, and aorta (von Hayek added) are presumably subject to similar circulatory influences during development so the ductus provides an exception to Benninghoff's generalization about the structure of blood vessels being a response to such influences, the anatomical arrangements of the ductus, in von Hayek's words, must be ' ortsgemass" rather than "kreislaufgemass" Like the structurally similar umbilical arteries, the ductus is *prepared for a single* post natal performance and is allowed no rehearsals for it

One point appears to have escaped von Hayek's *notice, namely*, that a short vessel like the ductus equipped with powerful, helicoidally arranged musculature must—one imagines—tend to decrease in length as well as in lumen when that musculature contracts provided the attachments of the vessel are sufficiently yielding It is the present writers' opinion that the ductus does in fact so shorten in the lamb, but satisfactory objective evidence, obtained before and after closure in *one and* the same animal, seems to be wanting On the other hand, the impression appears to be shared by Barcroft (1938, a, 79, fig 30) and by Boyd (personal communication) as a result of measurements in different but comparable, foetuses or newborn animals

If the full story of the ductus musculature *still* remains to be told, that of the innervation of the channel is not less incomplete Boyd's (1941) account was not specific to Man and will not therefore, be summarized here Mention may however, be made of the carotid body like tissue which forms a huge mass between the ductus and the aorta (its appearance in the human embryo was pictured by Boyd 1937, a) the histological character of the cells leads Boyd (personal communication, 1943) to suspect that they are chemo receptors They receive their blood supply from the pulmonary artery, the ductus, and the aorta, when they persist into adult life *as they* do—in part at least—in some species they are supplied by the aorta alone and not, as Nonidez has stated, by the pulmonary artery (Boyd, as before)

(xiii) THE ARTERIAL SUPPLY OF THE HEAD AND ARMS THE INTRA ABDOMINAL PORTIONS OF THE UMBILICAL ARTERIES

In the human subject, the single brachiocephalic artery of the lamb and other lower animals is replaced by the innominate left common carotid and left subclavian arteries, but this involves no functional change The only

follows is the result of an attempt to integrate a few of the more recent descriptions (Melka, 1926; Costa, 1930, 1931; von Hayek, 1935; Swensson, 1939; Boyd, 1941; Jager and Wollenman, 1942).

It is generally agreed that the ductus is looser in structure, and has more muscular and less elastic tissue, than the aorta or pulmonary trunk. The ductus consists of an intima, ending at a well-defined internal elastic membrane, a media, and an adventitia. According to Costa (1930), the width of the media at term is about the same in the ductus and the aorta; the intima, on the other hand, is about one-third as wide as the media in the ductus, and about one fifteenth as wide as the media in the aorta. In addition to being of great relative thickness, the intima of the ductus varies considerably in width in any given transverse section, and also in different portions of the same specimen. The variations are due to protuberances on the inner aspect, and the lumen of the channel is correspondingly uneven. The protuberances vary in number, width, and length; they are formed mainly of fine elastic fibres and longitudinal muscle fibres, with endothelium on their inner aspect and often some splitting up of the internal elastic lamina on their outer aspect. How far they are apparent in a patent ductus is not clear, but one cannot help remembering that the umbilical arteries are not ridged internally, by similar projections, in the normal state (Bondi), though they do have irregular lumina in the contracted state. The elastic fibres of the intima are said to connect up with those in the corresponding layer of the pulmonary trunk and aorta. According to Costa, the intima of the ductus contains much mucoid substance, a precursor of the elastic tissue which is to be concerned much later in the post-natal anatomical closure of the channel. The media of the pulmonary trunk and aorta is compact and composed of laminated bundles of dense elastic fibres; that of the ductus, by contrast, is loose in structure and consists mainly of smooth muscle, with some fine, wavy, and less regularly arranged elastic fibres; delicate collagen fibres are present in the interstices between the muscle cells (Costa) and there is also some collagen next to the adventitia. Mucoid substance is present but to a lesser extent than in the intima (Costa). There is no external elastic lamina. The adventitia is not unlike that of the pulmonary trunk and aorta; it contains collagen, some elastic fibres, and a few or no smooth muscle fibres. There are numerous vasa vasis, and some of them give off branches to the outermost part of the media; on the whole, the nutrition of the ductus is as well catered for as that of the aorta.

The transitions in structure at the unions of the pulmonary trunk with the ductus, and of the latter with the aorta, do not appear to have any special bearing upon the functional story, so readers may be referred to Melka, Costa, Swensson, and Jager and Wollenman for details. On the other hand, the musculature of the media and the innervation of the ductus do require further consideration. Melka described the media as containing three layers of muscle. Costa said that the inner two-thirds of the media are occupied by a circular muscle layer separated sharply, though not by elastic or connective tissue, from a more external oblique or longitudinal layer. Swensson said that the longitudinal musculature is especially concentrated on the side next the aorta, where it alternates with circular muscle; it is very marked next to

CHAPTER X

The Course of the Blood Flow in the Human Foetus

In order to parallel Chapter IV, a separate Chapter has been allotted to statements about the course of the blood flow in the human foetus. There is, however, practically no direct evidence about the living human subject, and ideas based upon post mortem injections and measurements are not a satisfactory substitute for such evidence. On the other hand, realization of present ignorance is perhaps the necessary prelude and stimulus to further research, so it is of use to review the statements found in the literature.

In 1835 (as mentioned in Chapter I above), John Reid published the results of injection experiments carried out upon three dead foetuses. The injection for the inferior vena cava was coloured red, that for the superior vena cava yellow. In the first foetus (4 months) the superior injection failed to pass, and the inferior one was small in amount. Some of it went into the right atrium but none into the right ventricle; the bulk went through the via sinistra and filled the whole of the left side of the heart. In the third foetus (7 months) all the superior injection (and a minute fraction of the inferior injection) went to the right side of the heart, whence it was distributed to the pulmonary arteries and, via the ductus arteriosus, to the descending aorta and its branches. All but a trace of the inferior caval injection, on the other hand, passed to the left side of the heart, the first part of the aorta, and the vessels supplying the head and upper extremities. In the second foetus (full term) the picture was similar, except that there was somewhat greater admixture of the red and yellow streams. On the basis of this small number of post mortem injections Reid concluded that the blood returning from the placenta passes principally to the head and superior extremities, and he thought that the purpose of the arrangement might be to ensure that the brain received the best aerated blood available.

Ziegenspeck (1905, 415) examined a large series of fixed foetuses and reported findings which differed from Wolff's earlier ones (1776), in respect of the inferior caval channel. For in Ziegenspeck's specimens the left opening of the channel was always narrower than the right, and there was little change from the 7th week of intra uterine life onwards. In his schema of the foetal circulation (ibid., 420) he postulated an equal division of the inferior caval blood flow, half going to the left and half to the right (fig. 10). A full account of the schema need not be given here, for its disregard of certain foetal flows invalidates it from the outset (see Chapter I), and there is, therefore, no need to adduce further possible criticisms of it. So far as one can gather, it never gained any wide degree of acceptance.

Patten's (1933) post mortem measurements in a large number of foetuses led him to favour the idea of a mixing of the inferior and superior caval blood streams within the right atrium. This concept appears to be ruled out of

other arteries that call for special mention are the umbilical ones which, in the human foetus as in the foetal lamb, are the large terminal branches of the descending aorta Here only their intra-abdominal portions will be described, the extra-abdominal ones have already been dealt with in section ii above

Macroscopically, the intra-abdominal portions are yellowish red in colour, their walls are more compact than those of the cord arteries (Strawinski, 1875) The proximal stretches (up to the bladder) are obviously less contractile than the distal ones (from the bladder to the umbilicus), for in stillborn infants or those which die soon after birth the proximal stretches are patent and full of unclotted blood, while the distal stretches are contracted and empty of blood or else contain a thread-like clot (Bondi, 1905) There is a gradual change-over from a typical arterial structure to one approximating to that of the cord arteries The thickness of the vessels increases up to just proximal to the umbilicus, and the musculature at this point is wider than anywhere else inside or outside the abdomen (Strawinski) The internal elastic lamina tails off towards the umbilicus, pari passu with the appearance of longitudinal muscle (Bondi, 1905), or perhaps it is more correct to say that it splits up to surround this muscle (Kopp, 1937) The elastic tissue falls off in amount, the muscular tissue increases Towards the umbilicus, also, the adventitia has less elastic tissue and smooth muscle and fewer vasa vasorum, but is richer in loose, wide-meshed connective tissue containing mucoid substance In other words, it shows an increasing resemblance to the tissue of Wharton's jelly (Bondi, 1905) There is usually one main nerve to each artery, according to Schott (*1836, quoted by Goenner, 1906*), *in the female it comes from the* lateral uterine plexus, in the male from the rectal plexus The trunks and fibres are non-myelinated, and in some areas form larger or smaller meshes (Spivack, 1943)

So much for the general picture, for details one can go to Bondi (1905) In the proximal stretches the arterial media contains circular muscle bundles *and the adventitia longitudinal ones The elastic tissue is plentiful* Near where the superior vesical arteries are given off, the main arteries show little difference in structure, the chief one being the appearance in places of longitudinal muscle bundles internal to the circular muscle When the arteries are contracted, this longitudinal muscle protrudes into the lumina In places, too, the media already shows the loose interfascicular tissue which is so typical of the cord arteries The terminal stretches of the intra-abdominal vessels are in many respects similar to the cord arteries The lumina of the contracted vessels are almost invisible and vary in shape according to the *number of projections* caused by the inner, longitudinal musculature External to the longitudinal muscle, etc, are thick circular muscle bundles loosely joined by plentiful connective tissue The adventitia is very wide, its inner part is composed of very loose connective tissue and has no muscle fibres Wide vasa vasorum and isolated nerve fibres are present

The general plan of the musculature in the distal stretches of the arteries was found by von Hayek (1935) to be similar to that in the cord arteries, and it has already been summarized in section ii above Long before, Hofmann (1877) had concluded that the " longitudinal " muscle was spirally arranged

have applied the Nuffield Institute findings from the sheep foetus to the human foetus, yet he makes the inferior caval blood pass through the right atrium to reach the left atrium and shows thereby that he has not grasped the functional significance of the crista dividens[1] Farther on, he says that Barclay et al have not given exact quantitative figures for the amounts of inferior caval blood passing right and left respectively That is literally true, for the cineradiographic apparatus is not a Stromuhr, on the other hand, Barclay et al have quite clearly shown and stated, that the bulk of the inferior caval flow passes to the left side of the foetal lamb's heart It would be legitimate to say that this finding may not be applicable, without more direct authority, to the human foetus, but it is certainly incorrect to override it in respect of the sheep foetus

Bonin s own concept of the foetal circulation seems to be born of his aversion to Sabatier s belief that certain parts of the body are supplied with more highly oxygenated blood than others The new schema is based partly on anatomical measurements (including those of Patten) in human foetuses and partly on experimental findings (e g those of Hamilton, Woodbury and Woods Barclay et al Windle and Becker) in the living foetuses of lower animals Strangely enough Bonin accepts the course of the superior caval flow as demonstrated by Barclay et al and by Windle and Becker in these lower forms but rejects their findings, derived from the same or similar experiments in respect of the inferior caval flow In place of these direct observations on living foetuses of lower animals, he makes calculations from post mortem measurements in human foetuses, and concludes that the inferior caval flow is so distributed that the right ventricular blood is as rich in oxygen as the left ventricular blood For all that has been *proved* to the contrary, this may be true in the human foetus But comparisons of cineradiographic records of living sheep foetuses with even immediate post mortem measurements in the same animals have many times shown how unreliable such measurements can be as a guide to the conditions obtaining during life So one may reasonably doubt if post mortem measurements in the human foetus are any more reliable

The extent to which the findings in lower animals can legitimately be transferred to Man is not altogether easy to assess, but it is probably better to approach the human foetal circulation along these lines rather than along those travelled by Bonin and it is largely for this reason that the available data have been collected together in the earlier Chapters of this book On the other hand the obvious anatomical differences[2] between the sheep and goat foetuses and the human subject make it desirable to extend the cineradiographic studies to primates which are as close as possible to Man Such extension is at present impracticable but it will doubtless be considered so soon as more normal conditions once again obtain

Even a primate study however though it is the natural next step, is not

[1] The special paper on it (Amoroso Barclay Franklin and Prichard 194) appeared only a month before Bonin s paper

[2] *E g* in the conformation of the lungs the length of the posterior/inferior caval channel the ... of the heart and so forth.

court by the correspondence of the cristae dividentes in Man and the lamb, and by the proved function of the ridge in the latter, i e that portion of the inferior caval blood which goes to the left side of the heart must go straight to that side and not first to the right atrium

Windle and Becker (1940, 424), and Fitzgerald and Windle (1942, 162) made a small but noteworthy beginning of a new phase by reporting incidental observations upon *living* subjects Windle and Becker opened the umbilical arteries in a four-months' foetus and injected Muller fluid into the umbilical vein in order to fix the central nervous system in situ The head and arms turned an orange colour before any change was visible in the abdomen and legs The authors considered that this observation, while it was no final proof, did at least suggest that the inferior caval stream goes directly, at this stage, to the left side of the heart Fitzgerald and Windle examined an anaesthetized, non-narcotized eight-weeks' foetus while it was still in utero The chorion was incised to display the specimen and it was seen that the umbilical vein blood was red in colour, indicating that the foetus was well supplied with oxygen from the as yet attached placenta

In cases where the via sinistra remains patent or partially patent after birth and a thrombus in the inferior caval system becomes dislodged, there commonly results a simultaneous embolism in both the pulmonary and systemic arterial systems (see, e g, Winkelbauer and Urban, 1929) One presumes that the dislodged clot is split by the crista dividens, part going to the left and part to the right, and this suggests that in foetal life the inferior caval stream is similarly divided, though not necessarily in the same proportions

Many writers have produced diagrams of the human foetal circulation It is necessary to remember that such diagrams are all hypothetical in the sense that there are as yet no direct records, obtained from living human foetuses, to serve as a basis for their construction Even so, many of the figures could be considerably improved by adequate attention to known anatomico-physiological facts which are unlikely to be altered by the findings in any direct records, e g the calibre of the pre-hepatic inferior vena cava should be depicted as less than that of the post-hepatic inferior caval channel

Bonin (1942), in a paper on the foetal circulation and its changes at birth, gave a description of Sabatier's schema, with evidence for it and objections to it, he then enunciated his own concept, which has in the main a morphological basis His description of the schema is at variance with the original (1774) account in respect of the calibre of the ductus venosus, for Sabatier said that this channel could transmit scarcely one-sixth of the umbilical venous flow, while Bonin changes this to the greater part of that flow His fig 1, also, incorrectly represents Sabatier's views about the anatomical dispositions of the atria

In the section detailing evidence in favour of Sabatier's concept, Bonin cites the publications made from the Nuffield Institute In Chapter IV above the present writers have raised general objections to citation along these lines, so some minor comments alone need be added here In his fig 2, Bonin claims to

have applied the Nuffield Institute findings from the sheep foetus to the human foetus, yet he makes the inferior caval blood pass through the right atrium to reach the left atrium and shows thereby that he has not grasped the functional significance of the crista dividens.[1] Farther on, he says that Barclay et al. have not given exact quantitative figures for the amounts of inferior caval blood passing right and left respectively. That is literally true, for the cineradiographic apparatus is not a Stromuhr; on the other hand, Barclay et al. have quite clearly shown, and stated, that the bulk of the inferior caval flow passes to the left side of the foetal lamb's heart. It would be legitimate to say that this finding may not be applicable, without more direct authority, to the human foetus, but it is certainly incorrect to override it in respect of the sheep foetus.

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Even a primate study, however, though it is the natural next step, is not

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[2] E.g. in the conformation of the lungs, the length of the posterior/inferior caval channel, the lie of the heart, and so forth.

necessarily the final one, for the chief value of the work on lower animals may well prove to be that a technique has been evolved which, *mutatis mutandis*, will prove suitable for the study of the living human subject It is, therefore, pertinent to conclude this Chapter by considering how far such a direct attack upon the problem is both possible and justifiable In as much, however, as this further research did not suggest itself as feasible until the text of this book was nearly complete, the notes which follow are merely preliminary considerations, unemended as yet in the light of any direct experience on the part of the writers

Some of the factors which would undoubtedly complicate a human study can be listed as follows

(1) The need for the parents' consent

(2) The necessity for asepsis

(3) The impossibility of delaying at will (as one can do in animal experiments) the onset of respiration

(4) Difficulties connected with the cineradiography

(5) Difficulties connected with the choice of a suitable contrast medium

(6) Difficulties connected with the technique of injection

As the above, and possibly other, factors are additions to the not inconsiderable difficulties attaching to the animal experiments described earlier in this book, it is necessary to discuss them in some detail and to see whether they preclude altogether a direct human recording or merely make it that much harder to achieve success

(1) The consent of some parents could, presumably, be obtained if they could be assured that the recording would be without danger to mother and child, or if it were known in advance that the foetus was abnormal (except in respect of its blood-circulatory system) and could not therefore, in any event, survive long after birth The former of these two possibilities is in large measure contingent upon the availability of a completely innocuous contrast medium, and it is very doubtful (see 5 below) if this condition obtains at the moment, though it may do so in the future For the time being, therefore, studies would probably have to be restricted to foetuses which, in respect of a system or systems other than the blood-circulatory one, were abnormal This would not only involve the assessment of the applicability of the results to the normal foetus, it would also mean conducting the research at a large maternity centre, at relatively long intervals, and over many months For foetuses of the type mentioned, which can be diagnosed as such before birth, are few and far between

(2) A preliminary survey suggests that asepsis could be attained, though its attainment would inevitably be rendered more difficult by the addition of the cineradiographic recording to the normal conduct of labour

(3) In the experiments upon sheep and goat foetuses, the fact that one could at will delay the onset of respiration (see Chapter II) extended very considerably the time during which the blood flow in the newborn foetus continued to follow its presumed intra-uterine course The fact that one could not so delay the onset of respiration in the human foetus means that one would, caeteris paribus, have to use more subjects to get the same amount

of information. For, with the onset of respiration, some of the mechanisms effecting the change-over from the pre natal to the post-natal course of the blood flow are set into action.[1]

(4) The difficulties which would attach to cineradiographic recording in a labour ward need not all be listed here. It suffices to say that they would be very considerable but not, so far as one can see, insurmountable. Inter alia, part of the apparatus would have to be kept in the labour ward until the whole series of recordings was complete, for it would be impossible to bring it in afresh each time a suitable case became available. If the obstetricians were agreeable to this deposit of apparatus in the ward, one would have to purchase a duplicate set-up for the purpose, but presumably the necessary funds could be obtained in view of the considerable scientific value of a successful outcome of the research.

(5) The difficulties connected with the choice of a suitable contrast medium form one of the chief stumbling blocks if, indeed, not the chief one of all. For, unless one can find a perfectly innocuous but at the same time effective medium, one will not be justified in recording the blood flow in *normal* human foetuses (see 1 above). As may be remembered, the radio opaque substance used in almost all the later experiments upon sheep and goat foetuses was 35 per cent perabrodil (diodrast). It was chosen because of its general lack of untoward effects and because of its rapid clearance from the blood, which meant that injections could be repeated at short intervals of, e.g., five minutes, thus permitting one to determine the approximate times of functional closure of the various special blood channels. A small number of human beings, however, are over-sensitive to injections of diodrast and in 666 800 administrations there were 10 immediate deaths, i.e. a mortality of 0.0015 per cent (Pendergrass et al., 1942). While there are tests for over sensitivity to the medium (see e.g. Archer and Harris, 1942, Robins 1942) they are not such as can be applied to the newborn child if one is to secure immediate cineradiographic records. And while a mortality of the low order mentioned might not preclude the use of a therapeutic agent, it would contra indicate injections of perabrodil into healthy human foetuses when the sole object of the injections was to assist in increasing scientific knowledge of the normal. So it is still necessary to find, or to select, an innocuous contrast medium which, by allowing one to study healthy rather than abnormal foetuses, would enormously shorten the total time required for the research and would make it unnecessary to assess the applicability of the results.

(6) Injections into the inferior and superior caval systems of the human foetus would have their own special complications not met with in experiments upon lambs and *kids*. So far as the inferior caval injections were concerned, the first complication would be *that* the length of cord available

[1] It is assumed throughout this *discussion* that the course of the blood flow, recorded so soon as possible after birth with the placental circulation continuing in vigour and pulmonary respiration not yet begun, is for *practical* purposes identical with the intra uterine course of the flow. The justification for such an assumption comes from the experiments on lambs (see Chapter IX, section x above).

was less than the full length[1] This would apply not only to deliveries per vias naturales, but also to those by Caesarean section, for in these latter a considerable length of the cord would be taken up before it had cleared the abdomen of the mother, who would be lying in the supine position and could not, as in the ovine experiments, be turned over on to her side The second complication would result from the fact that, while there are two veins in the lamb's cord, in the human cord there is only one So injections into the human umbilical vein would have to be made through a needle appreciably narrower than the vessel itself in order not to interfere at all seriously with the return of blood from the placenta In addition, subsequent haemorrhage from, or contraction of, this vein would have to be minimal It should not, however, be impossible for a careful and experienced person to ensure all this The superior caval injection, on the other hand, would presumably have to be made through the anterior fontanelle or into a jugular vein, the former route presents certain practical dangers which incline one to avoid it, and even the latter route is not one to be used lightheartedly by an unskilled person

From the above analysis, it appears that it would be very difficult, but not impossible, to secure cineradiographic records of the foetal blood flow (and of the immediately post-natal changes) in the human subject, but that the human studies should properly be preceded by primate ones, and that success would be materially hastened by the discovery of a perfectly innocuous contrast medium

So soon as normal human records have been secured and analysed, the true story can be published and illustrated, and the hypotheses and indirect evidence of the last three hundred years can be swept away With such an outcome as a possibility, there is certainly no lack of incentive to further effort, and one may reasonably suppose that this final study will, in the not too far distant future, be attempted

[1] In the experiments upon lambs and kids where delivery was by Caesarean section and the mothers were rolled over on to their sides after delivery the full length was available This not only facilitated the proper positioning of the foetus on the recording apparatus it also meant that the umbilical venae comites were as accessible as possible for injecting

[2] Actually it is doubtful if one would in any case be allowed to record the blood flow in foetuses delivered by Caesarean section partly because of the greater danger if asepsis were not absolute partly because of the mechanical difficulty involved in combining cineradiography with the conduct of an abdominal operation

CHAPTER XI

Certain Features of Human Birth

It is unnecessary to give here a full account of human birth, but it is of interest to describe two particular features of it, for they link up with what has gone before and with what is to follow.

(i) THE DIVISION OF THE UMBILICAL CORD

Very exceptionally in Man (chiefly primitive Man), the infant may retain for a while after birth its attachment to the placenta. Normally, however, the umbilical cord is ruptured or divided before the completion of the third stage of labour. Rupture is comparatively rare and is usually the result of precipitate birth: the breaking strain of the cord is reached through the sudden, heavy pull upon it. These cases, many of which come within the sphere of medical jurisprudence (Hofmann, 1877; Bayer, 1900), remind one, in so far as the strain on the cord is concerned, of the rupture occurring in animals such as the calf and foal. Commonly, however, the human cord is divided by the agency of assistants, and the points of interest are the means employed and whether or not division is preceded by ligation.

The ways in which more primitive peoples deal with the cord were described by Engelmann (1883), Ploss and Bartels (1897, 1908), and Rothrock (1939).[1] In a number of cases the procedure employed results in a mechanical stimulation of the ends of the divided vessels; it is therefore analogous to what occurs in certain lower mammals. Some races or tribes divide the cord directly the child is born; others wait for twenty to thirty minutes and then divide it whether or not the placenta has yet been delivered; others again wait until the placenta is out. The division is effected by relatively blunt but nevertheless cutting instruments (ordinary knives, the edges of palm leaf stems, sharp fragments of vessels or shells, bamboo splinters) or by grinding the cord between stones or by biting through it. Such crude methods are better calculated than a clean cut with a really sharp instrument to prevent subsequent haemorrhage, but further precautions are taken by some folk, e.g. the application of styptics (ash, powdered charcoal, vinegar, chewed up vegetable pulp) to the cut end, or the singeing of it in a flame, or its cauterization by means of red hot stones or animal bones. Only a very few people practise ligation of the cord with vegetable fibres or threads, or tie a knot in its free end, or twist the child round several times to effect torsion of the vessels.

When, as among the older civilizations, it became customary to divide the cord with a sharp knife or scissors, the mechanical stimulation to the ends of

[1] See also the letters of Price (1944) and Chesterman (1944). They formed part of a correspondence which was relevant to the subject of this section, but which appeared too late for adequate incorporation into the text. Those interested are referred to *Brit. med. J.*, 1944, 1, 77 and subsequent items.

the divided vessels was diminished. Hence there was increased danger of haemorrhage from them and ligation of the cord became a routine practice which has continued, with certain exceptions, to the present day. There is, however, a fair amount of evidence to show that the danger of haemorrhage from unligated cords is not so great as is generally supposed, and that ligation is necessary for the protection of a minority, rather than for that of the majority, of newborn children. According to Hofmann (1877), Ziermann and Wolfart carried out 1,500 deliveries in Berlin, in the early part of the nineteenth century, without tying the cord. J. Y. Simpson (quoted by Tait, 1876) rightly or wrongly correlated the closure of the umbilical vessels with the onset of an active pulmonary respiration, and wrote, "Hence various practitioners have gone so far as to aver that it is unnecessary, as a general rule, to place a ligature upon the foetal extremity of the cut umbilical cord if the cord be not tied till the child has cried loudly." Seitz (quoted by Rech, 1925, from Winkel, 1904), also, stated that untied cords usually do not bleed. But easily the most striking evidence is contained in a brief paper by Rachmanow (1914), who was convinced by the structure of the cord vessels in Man and lower animals that ligation was unnecessary, and thereafter proceeded to demonstrate the fact in several thousand confinements in a State Maternity Hospital in Moscow. As a result of five years' experience in over 16,000 confinements he concluded:

1. That non-ligation of the cord is a natural procedure and should be practised in all normal births of mature foetuses;
2. That it is not dangerous;
3. That it leads to better cicatrization of the umbilicus; and
4. That ligation is a therapeutic measure and must be reserved for pathological and exceptional cases (these formed between 10 and 20 per cent. of the series described in the paper).

The details of the technique employed are worth the attention of practising obstetricians but need not be quoted here. One ought, however, to inquire why a procedure, so firmly based upon the physiological properties of the cord vessels, has not been more universally adopted. The answer may be either that the literature upon the contractility of the divided, but unligated, vessels is not generally known, or else that the advantages of abstaining from ligation have not been regarded as adequate justification for a departure from the usual practice. If, however, abstention from ligation reduces the incidence of umbilical infection to the extent that Price (1944) has recently stated, there may be a prima facie case for a re-investigation of the whole matter. Should non-ligation be advocated in the light of the findings from such further study, one would still have to decide if it should be practised only in institutions, where adequate surveillance is possible, or if it could be extended to a proportion, at least, of non-institutional births. All that, however, is a business for the expert, and the present writers have fulfilled their task when they have drawn the reader's attention to the literature and to the problems arising out of it.

(ii) THE ONSET OF PULMONARY RESPIRATION IN THE NEWBORN INFANT

Barcroft (1942) was apparently, the first to describe different patterns which may be noted during the newborn infant's first essays in pulmonary respiration He listed three which he called the gasp the single prolonged inspiration, and the rhythm respectively , the first and second of these are associated with the occurrence of cyanosis during birth [1]

The gasp is the first type of respiratory movement which has been observed during the intra-uterine development of lower animals, and in them it replaces any type which is developed later, provided the brain is transected at an appropriate level [2] The inference is that gasping occurs in the newborn infant when the higher centres are put out of action by asphyxia, leaving the medulla in command of the functioning central nervous system This type of respiration is best and most often seen in the infant born with white asphyxia on account of tentorial tears and cerebral haemorrhage

The second type of movement namely the long drawn-out respiration, has no observed parallel in the early intra-uterine development of lower animals and has not been looked for in the more mature foetuses of such animals [3] It was associated in Barcroft's human series with a lower degree of cyanosis than was the gasping type

The third type namely rhythmical respiration, is associated with absence of cyanosis Its occurrence would appear to be dependent upon functional integrity of the pontine region and almost certainly of even higher parts of the brain It is seen most frequently in the infant which has experienced an easy delivery

The three types recall the gasping apneustic and pneumotaxic respiratory patterns observed by Lumsden (1923, 1924) in cats and lower animals at various levels of functional activity of the central nervous system They are also in line with the patterns seen during progressive poisoning with cyanide (Taylor and Barcroft 1929) or high concentrations of carbon dioxide (Barcroft 1942) Further they have been noted during resuscitation of patients whose hearts have failed under anaesthetics (see, e g , Bohn, 1939)

Barcroft concluded his account as *follows* ' Speaking generally, then, we may say that the type of respiration pattern is contingent upon the sensitivity of the nervous system at birth that this sensitivity is affected either by anaesthetics or by asphyxia the *higher parts* being more readily affected than the lower ones and that the more normal the condition of the *brain*, the earlier respiration will appear, and the more normal will be the respiratory pattern while the greater the degree of asphyxia the greater will be the abolition of function in the higher parts of the brain, and the greater the approximation to gasping in the respiratory pattern '

[1] The account which follows is based on Barcroft's short series of observations and *on other* unpublished ones made by Mr John Stallworthy F R C S *at the* Radcliffe Infirmary and elsewhere

[2] A presumably similar return to this primitive type of movement is seen in the adult human being dying from a pontine haemorrhage

[3] Colin (1873 871-2) however described what *sounds like it in a* 9 or 10 months foal delivered by Caesarean *section* *The foetus* he said came out with vivacity and began breathing deeply at long intervals

CHAPTER XII

Circulatory Changes Occurring During, and Shortly After, the Birth of the Infant

THE detailed story of the circulatory changes occurring during the birth of the lamb (Chapter VI) was in large measure based upon records, some of which have not yet been paralleled, and others of which are unlikely to be or cannot be, in the case of the human subject The only changes of note which can actually be seen in Man are the slowing down and arrest of the cord circulation, and the delivery of the placenta Certain additional data have been collected by other means, but even with these the total is far less than one could wish and in respect of a number of the birth changes one can only suggest what most probably happens It is quite largely with a view to making such suggestions as rational as possible that Chapters VII, VIII, and IX have been included *One has, however, constantly to bear in mind that the post mortem appearance of a vascular channel may be no real guide to its preceding functional state* This proviso applies particularly to those parts of the cardio vascular system which are more directly concerned with the change-over from the foetal to the post-natal conditions, and it means that large numbers of careful measurements listed in earlier publications may be valueless in the present connection, for they are post mortem findings and cannot be assumed to be identical with the in vivo measurements With this preliminary warning, one can proceed to notes about the individual changes in the human subject

(1) CHANGES IN THE HEART RATE

Krafka (1933) gave the ante-natal rate as 134, while Windle (1940, b) said that at term it is commonly between 130 and 150, with an extreme normal range of 110 to 180 While one may accept these figures, they are obviously inadequate for an understanding of the changes which occur at birth, and an attempt has, therefore, been made by the present writers to remedy this defect[1] In the first place, it should be realized that the extremes of normal range given by Windle are not due to some foetuses having a tendency to bradycardia and others a tendency to tachycardia For variations in rate of the order quoted above can, and often do, occur in one and the same foetus during the stages of its intra-uterine development They are caused in the main by extra-foetal activity, and may be regarded as changes from the fairly steady rate exhibited by the heart while the foetus is inactive and the uterus quiescent The extra-foetal activity may be of two kinds, namely, normal movement of a neighbouring maternal organ and manipulation by the obstetrician The uterine contractions which occur during the later weeks of pregnancy (and more particularly during labour) are typical examples of

[1] In making it they have drawn freely upon the wide personal experience of Mr John Stallworthy F R C S of the Radcliffe Infirmary Oxford

the former, they result in temporary diminutions of the foetal heart rate. Considerable slowing also occurs, as a rule, when attempts are made to alter the position of the foetus in utero by abdominal manipulation of the mother. The slowing occurs with or without anaesthesia, and the heart rate takes only a few minutes to return to approximately its previous level.

After birth, according to Krafka (1933), the heart rate is maintained at 170 to 180 for from 15 to 30 minutes, after which there is a slow and gradual deceleration. Windle (1940, b) added to Krafka's statement by saying that there is a slowing during birth but an acceleration with the onset of respiration. The cause of the slowing is uncertain. It can occur before the head is engaged, so compression of the head in the birth canal cannot be the explanation, or at least not in all cases. Among the other possibilities listed by Windle (1940, b) the one that seems most in accord with the known facts is that the heart is depressed by a decline in the oxygen saturation of the blood during labour; presumably the strong contractions of the uterus, after rupture of the membranes, interfere with the circulation through the placenta. The extreme example of this is seen in the foetus which dies in utero because the uterus fails to relax as it passes into the state of tonic uterine contraction. One is unwilling to accept the suggestion that the uterine contractions force more blood into the foetus and that the heart rate falls in accordance with Marey's law as the blood pressure rises, even though Windle considers that the full term blood pressure is high enough to evoke cardio-aortic and carotid sinus reflexes. For, in the first place, the blood pressure rise during human birth, even if one accepts Krafka's interpretation of Haselhorst's figures (see next section), is not over great, and after the initial slowing the heart accelerates for 15 to 30 minutes as mentioned above before decelerating gradually. It seems more probable that the initial slowing is due, as suggested, to cardiac depression and that the heart picks up as the cause of that depression is eliminated with the onset of respiration, possibly also because the cardio-accelerator centre is liberated from the effects of anoxia before the cardio-inhibitory centre. Later, with the progressive improvement in oxygen supply to the brain, reflexes effecting a slowing of the heart are established. The fact that the slowing occurs relatively later than in the lamb may be due to the greater maturity of the lamb at birth; indeed, this greater maturity should constantly be borne in mind when one is comparing the newborn infant with the newborn lamb. On the other hand, the blood pressure may rise more in the lamb on cessation of the placental circulation, and this may ensure a more rapid onset of activity in the cardiac centres.

(ii) CHANGES IN THE BLOOD PRESSURE

The arterial blood pressure of the human subject can be directly measured only in the cord arteries and even in these (unless delivery is by Caesarean section) only in the interval between the birth of the child and their functional occlusion. Ribemont (1879) and Haselhorst (1929, b) appear to be the only authors who have reported such pressure values.[1] Ribemont found an

[1] Krafka (1933, 1014) gave 60 mm Hg as the normal pressure at birth but it seems doubtful if this figure was the result of personal measurements.

average post partum value of 63 7 mm Hg while the placental circulation was continuing, the uterus was quiescent during the experiments Haselhorst recorded a steady pressure of 68 mm Hg in a pre-natal subject before delivery by Caesarean section The uterus was quiescent and the child was lightly anaesthetized via the maternal blood This is the only figure available for pre-natal arterial pressure Immediately after normal birth, in eight other subjects, the pressures were respectively, 84, 74, 62, 70, 62, 92, 46, and 110 mm Hg, giving an average of 75 mm Hg The onset of respiration caused no obvious change in pressure in these and in two other subjects, though a short cry did cause a temporary elevation of about 40 mm Hg in one of the latter Haselhorst, comparing the pre-natal value in the one case with the average post-natal value in the eight cases, came to the conclusion that there was no significant alteration at birth, especially as the average weight of the normally born eight was greater than that of the Caesarean infant and, caeteris paribus, there appeared to be a tendency for the pressure to increase with increasing weight Krafka (1933) proposed to disregard the three low values in Haselhorst's series on the ground that the artery might have become occluded between the needle and the umbilicus, if one does so disregard these three values, the average of the other five is 86 mm Hg, i e there is a rise of 18 mm Hg above the value for the Caesarean infant But it seems unlikely that Haselhorst would have overlooked such an occlusion of the umbilical artery It is more pertinent, in any case, to state that a single pre-natal record of the arterial pressure is inadequate as a base-line, obviously, many more determinations, both pre- and post-natal, must be made if one is to get any real idea of the changes during birth

In the lamb (see Chapter VI above) ligation of the cord may lead to a marked rise of blood pressure in the carotid and femoral arteries In the human subject Ribemont found that clamping of the cord 10 to 12 cm from the umbilicus resulted in a fall of pressure in the umbilical artery proximal to the clamp, the average initial pressure was 64 8 mm Hg and the average drop 16 6 mm Hg He attributed the fall to the loss of the extra-abdominal blood volume, for (1) it was more marked the earlier the clamping, and (2) it was greatest when the child did not breathe before the record began (Ribemont believed that respiration caused the placental blood to pass to the infant)

Haselhorst measured the pre-natal venous pressures in three mature foetuses, exposed by Caesarean section but still in utero The individual values were respectively 22, 34 to 30, and 24 mm Hg, average 26 mm Hg, the uteri were quiescent In the cords in which the average arterial pressure (see above) was 63 7 mm Hg, the average venous pressure found by Ribemont was 33 49 mm Hg In the clamped cords the pressure in the vein distal to the clamp rose by about 50 per cent through hindrance to the venous return

The above seem to be all the facts at present available about the blood pressure, and they are obviously inadequate as a basis for any wide generalizations Comparison with the findings in the lamb reveals a second feature of interest in addition to the one already mentioned, i e that the umbilical arterial pressure venous pressure ratio is very much higher in the lamb than

in the human subject Whether or not this is related to the difference in placental types one cannot say, at all events one is curious to learn the explanations of this and of the first difference mentioned above

(iii) THE SLOWING DOWN AND ARREST OF THE PLACENTAL CIRCULATION TRANSFER OF BLOOD TO THE NEWBORN INFANT CHANGES IN THE RED CELL COUNT AND HAEMOGLOBIN PERCENTAGE

1 *The slowing down and arrest of the placental circulation* —What one needs to know is the time that this takes, any general features, the mechanisms directly concerned, and the effective stimulus or stimuli

In normal birth (Bondi 1905) the first part of the cord to cease pulsating is the distal one, which is still in the vagina the arterial segments in it become thin hard cords[1] Then the pulsation ceases (5 to 8 minutes later) in the proximal portion About five minutes later again it has terminated at the umbilicus also The above picture is the rule in cases in which the child cries loudly some minutes after birth In a smaller number of cases in which the onset of respiration is delayed, the whole cord pulsates for about five minutes before the above sequence sets in Finally, in cases of precipitate birth, the first cry is uttered at once and the pulsation fades out so quickly that it is scarcely possible to follow the order of its disappearance Rech (1925) said that, with good respiration the pulsation ceases in 10 to 15 minutes, and the arterial closure is complete about 10 minutes later still Haselhorst and Trautwetter (1929) gave a range of from under 1 minute to over 15 minutes and Haselhorst and Allmeling (1930, see also Haselhorst, 1929 c), in a series of 120 cases found the upper limit about 30 minutes Windle (1941) said that normally the pulsation dies down not long after delivery of the infant and that thereafter there is a short interval before the placenta is delivered as a result of uterine contraction the average time for the whole process being about 10 minutes Ribemont (1879) also noted that an appreciable time elapses between the complete emptying of the arteries and the onset of uterine contractions

Before Bondi Hofmann (1877) had referred to the centripetal course of the arterial closure in view of observations by Baumgarten (1877) and himself he thought that it probably extends later to the distal sections of the intra abdominal vessels but that these are not involved *immediately* after birth in the prevention of haemorrhage from the divided cord Bondi (1905), apparently thought that they were Kleinwächter (quoted by Rech, 1925), however produced fresh evidence for the view that the contraction of the cord arteries is the essential part of the story Normally, some placental circulation can continue for a while after delivery of the child, in the first two minutes for instance (Haselhorst, 1929, b) the oxygen content of the umbilical vein blood may rise to three times its initial post partum level

[1] It is somewhat surprising that the contraction should begin at this end where the arterial musculature is only half as thick as it is at the foetal end of the cord (Strawinski 1875) and correspondingly less powerful (Krafka 1933) Obviously other factors than the actual strength of the vessel walls are involved

Owing to their structure the arteries of the cord can contract right down. Where it is present, the inner longitudinal muscle thickens and projects into the lumen. These projections, in consequence of the simultaneous contraction of the outer circular musculature, make the arteries completely impervious, and it needs a relatively enormous pressure, especially in the proximal portion of the cord, to reopen them. Krafka (1933) found that at the foetal end of a cooled exsected cord they resisted completely a perfusion pressure of 250 mm. Hg, and that even towards the placental end the flow under this pressure was small. The resistance was in the arteries themselves; dissecting them free from the cord matrix made no difference. Sometimes the contractility of the arteries is sub-normal, e.g. in weak, premature, or undernourished infants; in such cases there is increased danger of haemorrhage from the divided cord. At other times, the initial closure is effective, but for one reason or other the musculature relaxes some time after birth (as it can do on occasion in the ductus arteriosus of the lamb). Normally, however, the closure is both effective and permanent.

Various factors have from time to time been mentioned as concerned, or possibly concerned, with the arterial closure. These are:

(*a*) Thrombosis.

(*b*) Fall of blood pressure after birth.

(*c*) The increased oxygenation of the blood resulting from the onset of pulmonary respiration.

(*d*) Mechanical stimulation.

(*e*) Cooling.

These may be considered in order.

(*a*) *Thrombosis*.—This was first suggested, it would appear, by Virchow (1851), but the evidence is predominantly against this being a factor of any importance, and the coagulation time is well above the adult value for 10 to 15 days after birth (Rodda, 1920; Lucas et al., 1921, quoted by Krafka, 1933).

(*b*) *Fall of blood pressure after birth*.—This is the old hypothesis of B. Schultze (1871), who thought that after birth, with the opening up of the lungs and the closure of the ductus arteriosus, there would be less blood in the systemic circuit and less force (left ventricle only instead of both ventricles) to impart a pressure to it in the descending aorta. In a stillborn foetus Krafka (1933) found the haemoglobin content of the lungs, the rest of the body, and the cord plus placenta to be respectively 5.31, 65.19, and 29.50 per cent. of the whole. As most of the extra-foetal blood (see below) is normally transferred to the newborn infant if the cord is ligated late, it is obvious that the expansion of the lungs can have little effect upon the available blood volume (actually, it has not yet been shown to have any). Ribemont (1879) found that the umbilical arterial pressure fell after birth only if the cord was ligated early (the earlier the ligation the greater the fall); as time is usually allowed for the transfer of the placental blood, a fall in blood pressure cannot normally be concerned in the arterial closure.

(*c*) *The increased oxygenation of the blood resulting from the onset of pulmonary respiration*.—J. Y. Simpson (quoted by Tait, 1876) and Tait himself remarked upon the interdependence of respiration and the disappearance of

pulsation in the cord arteries Bondi (1905) explained his various clinical observations in relation to the effectiveness or otherwise of the child's respiratory efforts, but he accepted Schultze's hypothesis of the interrelation between respiration and blood pressure Rech (1925) on the strength of his perfusion experiments, concluded that the post natal rise in the blood oxygen with the onset of respiration was the prime cause of the arterial closure Haselhorst (1929, b), however, found no regular relation between this onset and the cessation of flow through the arteries, the vessels can on occasion contract down before breathing has begun, or continue to pulsate a considerable time after it has become established

(d) *The effect of mechanical stimulation*—That this form of stimulation can result or aid in closure of the umbilical vessels is obvious from what has been written in the last Chapter about the division of the cord among some primitive peoples The data about civilized peoples include the following Schröder (1871 quoted by Hofmann 1877) said that haemorrhage is an infrequent occurrence following rupture or tearing of the cord but is an almost invariable sequel to a clean cut through it Hofmann himself was unable to recollect any definite case of haemorrhage in a series of clandestine births, though the cord was usually severed close to the umbilicus or on occasion, actually torn out from it, it is known that mechanical stimulation tends to be considerable or even severe in such births Bondi (1905) noted the rapid arrest of the placental circulation in precipitate births but said that the cord was not necessarily ruptured obviously, it is so in some cases and it may be mechanically stimulated to an appreciable extent though not up to the point of actual rupture in others Rech (1925) was predisposed by his own work to explain the contraction of the cord arteries as the result of increased oxygen supply to them and he was therefore inclined to minimize mechanical stimuli as a factor He noted no contraction on cutting through a perfused stretch of cord artery and he said that precipitate birth involving tearing of the cord results in no haemorrhage provided respiration has been efficient Haselhorst (1929 b) found that section of the cord caused a local contraction of the arteries but that they continued to pulsate freely between the cut and the umbilicus The procedure could be repeated several times if one began 30 cm from the abdominal wall and made a fresh cut through the pulsating stump after each arrest of haemorrhage from the divided end of the cord On the whole of the evidence it would appear that mechanical stimulation plays an important part in some births a minor part in others and probably no part or quite a negligible part, in a considerable number

(e) *The effect of cooling*—One must agree with Bondi (1905) that this is of no great importance during actual birth if, as he alleged, the contraction of the umbilical arteries commences in the more distal part of the cord while it is still in the uterus and vagina and practically unexposed to cooling Bayer (1900) had noted earlier that cold could not be operative in the special cases in which the cord ruptures while the foetus is still in the uterus or birth canal One may also point out that the sheath and outlying matrix of the cord must be cooled before the arteries can be affected and that there is a copious placental circulation keeping up the vascular tempera-

Owing to their structure the arteries of the cord can contract right down Where it is present, the inner longitudinal muscle thickens and projects into the lumen These projections, in consequence of the simultaneous contraction of the outer circular musculature, make the arteries completely impervious, and it needs a relatively enormous pressure, especially in the proximal portion of the cord, to reopen them Krafka (1933) found that at the foetal end of a cooled exsected cord they resisted completely a perfusion pressure of 250 mm Hg, and that even towards the placental end the flow under this pressure was small The resistance was in the arteries themselves, dissecting them free from the cord matrix made no difference Sometimes the contractility of the arteries is sub-normal, e g in weak, premature, or undernourished infants, in such cases there is increased danger of haemorrhage from the divided cord At other times, the initial closure is effective, but for one reason or other the musculature relaxes some time after birth (as it can do on occasion in the ductus arteriosus of the lamb) Normally, however, the closure is both effective and permanent

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Budin (1876 quoted by Ribemont, 1879) found that the average amount so transferred was about 92 g, and Ribemont considered that the transfer is effected as a result of the onset of respiration, it is not due, he said, to uterine contractions, which usually develop later Cohnstein and Zuntz (1884) gave the amount transferred as 60 to 100 g, representing an increase of about one-third in the infant's blood volume Haselhorst and Allmeling (1930) analysed 120 cases in which ligation was practised at varying intervals after birth, and found that the longer the delay the more complete is the transfer On the average, with the necessary time allowed, 98 g blood pass to the child leaving 67 g in the placental circuit (incidentally, the lowness of this second figure shows the efficiency of the functional closure of the cord and placental vessels) Later work has confirmed the earlier findings (literature in DeMarsh Alt, Windle and Hillis, 1941 Wilson, Windle and Alt 1941, Windle 1941) and one can say that about 100 c c is transferred if the cord is ligated late, this amount represents about one-third of the child's blood volume[1]

3 *Changes in the red cell count and haemoglobin* —Except where otherwise stated the following account is derived mainly from the publications of Windle and his colleagues (i e from the papers just mentioned, and from Windle 1940 b) At the end of gestation (i e in blood taken from the umbilical cord at the moment of birth) the red cell count is of the order of 4 48 millions per cu mm Within about an hour this figure increases to 5 45 millions per cu mm in an infant whose cord has been ligated at birth, and to over 6 millions in an infant whose placental blood has been conserved to it by late ligation of the cord The post natal increase of 1 million (if one excludes for the moment that due to placental blood) is not yet fully explained but it is suggested that it may be due in part or in whole, to expulsion of concentrated corpuscles from the spleen

The average diameter of the foetal red cell decreases during gestation, but is still perceptibly greater at full-term than it is in post-natal life The amount of haemoglobin per 100 c c increases during gestation and at birth is 15 7 g Within about an hour this figure has risen to 19 5 g in cases in which the cord has been ligated early, and to 22 1 g in cases in which ligation has been delayed The reticulocyte count is lower during the first week of post natal life in these latter i e they do not require to be so actively haemopoietic Further through subsequent breakdown of the excess blood they secure a reserve of iron, and possibly of other substances, to carry them through the difficult first six to twelve months of independent existence

(iv) THE FUNCTIONAL CLOSURE OF THE DUCTUS VENOSUS

The anatomical similarity between the human and ovine foetuses in respect of a lipping at the beginning of the ductus venosus makes it reasonable to suppose that the functional closure in each is a similar process, i e that it is effected by a sphincter mechanism within a matter of minutes from birth

[1] This fact should be remembered for there is often a tendency to ligate the cord prematurely particularly when the child is delivered by Caesarean section

ture from the inside That the divided but unligated cord reacts to cold by contraction was shown by Haselhorst (1929, b), but that, of course, is no proof that cooling plays a part during normal birth When the severed cord was put into water at 20° C, there was a short-lasting haemorrhage from the three vessels, that from the vein ceasing first When it was exposed to air at 20° C, the arrest of haemorrhage was more rapid, and that from the arteries ceased first, Haselhorst ascribed the priority of the arteries in this second case to their greater sensitivity to the oxygen in the air

The effects of warmth upon the divided but unligated cord have been tested by putting the stump into warm water Schulze (quoted by Hofmann, 1877, from Mende, 1819) reported absence of haemorrhage, and Ahlfeld (quoted by Krafka, 1933) actually saw the arteries contract down during the development of respiration when a child was delivered into a warm bath On the other hand, Stutz (1878 quoted by Henneberg, 1900), Lindemann (1880, quoted by Bayer, 1900), Cohnstein and Zuntz (1888), Bucura (1902), Bondi (1905), and Haselhorst (1929, b) all reported reopening of previously contracted arteries on exposure to warmth On the evidence, one may believe that the vessels on occasion contract down too strongly to be relaxed subsequently by warm baths or clothing, while the reverse may obtain in other cases up to several hours, or even some days (Stutz), post partum

A *reflex contraction of the cord arteries in response to cooling of the skin* and respiratory passages was suggested as a possibility by Strawinski (1875), but it is ruled out if one accepts Spivack's (1943) conclusion that these vessels are not innervated, it is not ruled out in the case of the intra-abdominal portions of the umbilical arteries, which are innervated, but little has been recorded about the reactions of these portions

The closure of the umbilical vein after birth has been relatively little studied Until the cord arteries are completely occluded, there is a return flow through the vein (Haselhorst, 1929, b) and, even when the former are completely impervious, the latter still has a small lumen (idem, 1929, a), which exhibits none of the irregularity commonly found in those of the contracted arteries From the point of view of the transfer of the extra-abdominal blood to the newborn child, it is an advantage that the vein is less contractile than the arteries The blood does not usually flow back out of the severed vein, but it can do so if the child is asphyxial or if there is mechanical compression of its upper abdomen or lower thorax (Hofmann, 1877) Ribemont (1879) described three cases in which turgid veins were promptly emptied of blood as a result of one or more inspirations One can assume therefore that, if the onset of respiration increases the pressure gradient from cord to heart, and the heart is healthy and able to clear the blood brought to it, there will be no haemorrhage from the severed vein and its wall, when the blood has passed on, will tend to collapse on itself The intra-abdominal portion, examined some time after birth, is collapsed and shows no indication of contraction (Bondi, 1905)

2 *The transfer of blood to the foetus*—If the pulsation is allowed to cease before the cord is ligated, there is a transfer of blood from the placenta and the extra-abdominal portion of the umbilical vein to the newborn child

mined by means of cineradiography or some equivalent technique. Until that has been accomplished, the reader must decide for himself how far he is justified in applying to the newborn human being the closure times reported for the lamb.

(vii) INEQUALITY OF CHANGE IN THE MUSCULATURE OF THE TWO VENTRICLES

Keen (1942; see also Ziegenspeck, 1905, Table III) found that the planimetric ratio between the right and left ventricular walls was 1 : 1 in full term and immediately post natal hearts, but that so early as six days after birth the ratio became 1 : 1.35 and that thereafter the preponderance of the left ventricular wall became even more marked. Transverse sections at arbitrary levels are, however, no guide to the respective weights of the two ventricles even if they suggest the tendency of one ventricle to hypertrophy relative to the other.[1] From other sources comes evidence that the right ventricle retains a foetal dominance for some time from birth, after which the left ventricle predominates for the rest of life in the healthy subject. This evidence is electrocardiographic and anatomical. The electrocardiogram of the human infant (Lewis, 1913–14, 1920; Krumbhaar and Jenks, 1917; Herrmann and Wilson, 1922) exhibits a right axis deviation up to two or three months from birth. For the term "right axis deviation" one can substitute, in this instance, the term 'right preponderance' (Carter, 1937, 44) because during the period mentioned the right ventricle actually weighs more than the left ventricle (Lewis, 1920). In full term foetuses, according to Patten (1933), it is 13 per cent heavier. The change to "left preponderance" cannot be regarded as a very immediately post-natal one, but it is necessary to give this brief account of it, as it may need to be taken into consideration in connection with the post-natal closures of various foetal blood channels. According to Seham (1924), the heart is at its greatest proportionate development at the time of birth, when it contributes 0.86 per cent of the total body weight, as compared with 0.52 per cent in the adult. The illustrations in Keen's paper give the impression that the walls of the infant's right ventricle undergo a relative diminution in thickness for some time after birth.

[1] The present writers had the intention of comparing the thicknesses of the walls in all available foetal hearts some time before Keen's paper appeared, but were dissuaded by the impossibility of deciding which were comparable sections of the two ventricles.

Farther than that one cannot at present go, and it seems improbable that any more direct approach will be possible in the immediate future

(v) THE FUNCTIONAL CLOSURE OF THE VIA SINISTRA

In ± 1 per cent of any large number of hearts, functional closure of the via sinistra is impossible because of congenital defects in the structure of its pars libera (Patten, 1931) About the closure of the channel in the remaining ∓ 99 per cent there are conflicting views

The earlier approach to the problem was made through analyses of post mortem measurements, the best known being those published by Patten and his collaborators Patten himself produced a graph (1931, fig 8) showing respectively the rate of functional closure (which was "based on circumstantial evidence and should be regarded as tentative"), the rate of reduction in size of the opening into the left atrium, and the rate of anatomical obliteration of the channel He considered (ibid, 40–41) that functional closure had occurred when, in a post mortem specimen, the pars libera viae sinistrae lay tightly against the interatrial septum, even though a probe could still be passed between the two This stage was reached, he stated, by about the end of the first post-natal month

Because of their experience with newborn lambs, the present writers are quite unable to accept this criterion of functional closure of the via sinistra For the channel was definitely impervious to any blood flow (as shown by the cineradiographic records) in a number of lambs, but the post mortem measurements in these same animals would have made Patten conclude that no functional closure had yet occurred in them

The final answer to the question, "When does the human via sinistra functionally close?", must be obtained, one imagines, by means of cineradiography or some equivalent technique Until then the reader must decide for himself how far he is justified in applying to the newborn human being the closure times reported for the lamb About the factors concerned in such closure it may be more possible to speak when more experimental evidence has been obtained from lower animals

(vi) THE FUNCTIONAL CLOSURE OF THE DUCTUS ARTERIOSUS

Gerard (1900) drew a clear distinction between the immediate functional, and the considerably later anatomical closure of the human ductus arteriosus A number of hypotheses have been put forward in respect of the mechanism of the former (see, e g, Wells, 1908, Graper, 1921, Swensson, 1939), but the general similarity of structure exhibited by the channel in the lamb, kid, and human subject makes it appear probable that the closure in the last-named occurs in much the same way as it has been shown to do in the two first-named There is also considerable structural similarity between the ductus and the cord arteries, so such information as exists about the functional closure of the latter may help one to envisage the similar closure of the former The time of functional closure will, eventually, have to be deter-

exist in the liver cells supplied respectively by the two streams But these researches and others which we have not mentioned, are at present held up, or at best are only proceeding slowly, either because of lack of subjects or else because of other more immediately urgent, calls upon our time

The fact that in Chapter II we felt compelled to lead through the adult to the foetus is to some extent a reflection of, and upon, the current order in which knowledge about these is imparted in human anatomy courses The terms in use for certain parts of the foetal cardiovascular system are similarly witness to the fact that the description of the foetus commonly follows, instead of preceding as logically it should that of the adult Sabatier, in his *Traite complet d'anatomie*, included both foetal and adult matter in his descriptions of the heart etc , and did so in a way that demonstrated the unity of the whole story But even he did not invariably, or even commonly, follow the logical order, and describe first the foetus and thereafter the post natal subject Physiologists are even worse offenders than the anatomists, for they either omit altogether any reference to the foetus, or else give too brief an account of it The matter is one for concern, when so much more is now known about foetal anatomy and physiology and when the post natal consequences of pre natal abnormality are so much better understood Surgeons are awakening to the importance of such correlation since Gross and his colleagues described the first successful ligation of a patent ductus arteriosus (Gross 1939 a, b, Gross Emerson and Green 1939 Gross and Hubbard, 1939), a quick look through the appropriate pages of the *Quarterly Cumulative Index Medicus* shows how Gross lead is being followed in his own and in other countries

Our experimental results to date are a direct contribution to veterinary physiology but our main desire is to know better what happens in the *human* subject With this object in view, we have compared the cardiovascular system of the sheep foetus with that of the human foetus, and have formed some idea as to how far the physiological findings in the former can reasonably be applied to the latter Such a procedure has often been followed in attempts to ascertain the physiology of Man and textbooks on the subject contain numerous examples where transfer of findings from lower animals has, with or without adequate justification been effected In the matter under review however we have felt that an estimate, based on comparative anatomical studies is very much a personal judgment We have, therefore refrained from giving our own view in the text of this book and have contented ourselves with summarizing the facts which the reader should have at his disposal in making his estimate In other words, we consider that this method of approach to the physiological story in Man is not likely to produce any universally convincing or final statement, though with the extra facts as a basis, it may produce one that is nearer to the truth than were its predecessors Indeed so far as the living human subject is concerned, the chief value of our work on lower animals may well prove to be that we have evolved a technique suitable for the study of the newborn infant both before and after the functional closures of the special foetal blood channels There is however no need to elaborate on this for the matter has already been discussed at sufficient length in Chapter X above

PART SIX

CHAPTER XIII

Concluding Remarks

WE could, without risk of criticism, have ended this book when we had penned the last words of Chapter XII But we felt that it was right to add certain notes and reflections derived from our researches of the last six years, for studies of even this relatively short duration have inevitably made us far better acquainted than the average reader can be with things foetal, and our experience may be of aid to others who wish to work in this field

In the first place, our historical studies have not only provided us with many of our agenda, they have also given us certain warnings and a proper outlook upon our own results The more important warnings are that too much reliance should not be placed upon isolated observations, and that schemata which are based solely upon post mortem measurements of vascular channels, or which fail to take into account all the foetal blood flows, may on occasion be grossly misleading Ziegenspeck (1905) criticized Kilian on the first count, but is personally open to indictment on the second and third ones We ourselves have reported findings in single specimens of certain genera, but we have endeavoured not to build too heavily upon what might be inadequate bases We have also, in places, given post mortem measurements of vascular calibres, but we fully realize that such need confirmation, whenever possible, from records of the living foetus On the other hand, given this proviso, it would have been wrong to omit such details where their introduction was pertinent to the story

So *much for the warnings derived from the history of our subject* The outlook which it gives us upon our own experimental results need not take long to describe By our precise cineradiographic recording, we have substituted a measure of certainty for the ignorance confessed by Bichat (1801),[1] and for the hypotheses or indirect evidence of later writers But our records are not of the foetus actually in utero, further, they have been almost entirely confined to one genus and are incomplete of even that one , finally, improvements in the apparatus or the introduction of new techniques may, sooner or later, make possible *a far more detailed story than any we can at present* produce While, therefore, we can claim to have made a beginning, we are fully aware that it is only a beginning[3]

When opportunity allows, we intend to study, inter alia, the comparative physiology of the umbilical-portal venous distribution within the liver, at the same time a colleague will determine any biochemical differences which

[1] Une voile est encore répandu sur la circulation du fœtus

The blood flow through the head the upper and lower extremities and the placenta has still to be recorded

[3] Our attitude towards the physiology of the foetal circulatory system is very like that of Vesal (1564) towards its anatomy Fassus me in multis quæ ad fœtum spectant non mihi satisfacere

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Our results as a whole are a striking demonstration of the value of radiographic, and especially cineradiographic, studies of the normal subject, and of the impetus which such studies can give to research in the allied fields of anatomy, physiology, and so forth When the West Wing of the Nuffield Institute was assigned to research by means of cineradiography and allied techniques, few—even of our friends—were optimistic about our chances of success It seemed to us, however, that there were definite possibilities in quite a number of fields, of which the physiology of birth was one, and we have been gratified by the results so far obtained in our various investigations We plan in the future to continue experimental work in parallel with a more scientific study (see Barclay, 1943) of the radiological normal Further than that we need not discuss our objectives, and at this point we may fittingly conclude not only this discussion, but also this book

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